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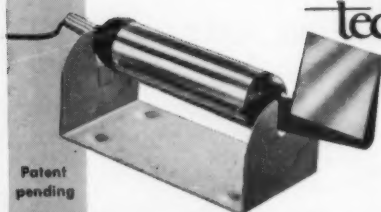
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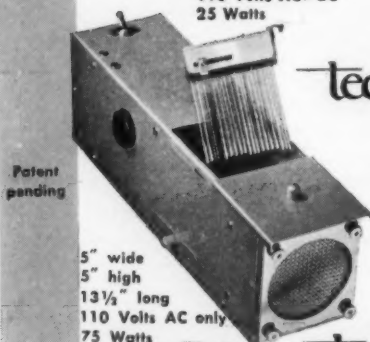


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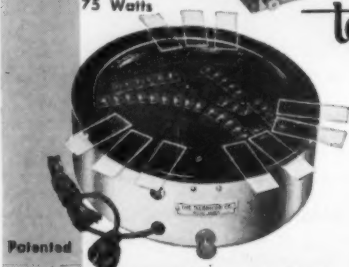


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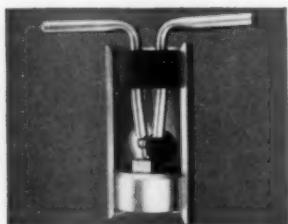
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THE TRANSISTOR

A picture report of progress



FIRST TRANSISTORS were of this point contact type (picture about twice life size). Current is amplified as it flows between wires through a wafer of germanium metal. These transistors are now being made at the Allentown plant of Western Electric, manufacturing unit of the Bell System. They will be used in a new selector which finds the best routes for calls in Long Distance dialing.



NEW JUNCTION TRANSISTORS, still experimental, also use germanium but have no point contacts. Current is amplified as it flows through germanium "sandwich"—an electron-poor layer of the metal between two electron-rich ends. This new transistor runs on as little as *one-millionth* of the power of small vacuum tubes.



MUCH HAD TO BE LEARNED, especially about the surface of germanium and the effect of one part in a million of alloying materials. Transistors promise many uses—as amplifiers, oscillators, modulators . . . for Local and Long Distance switching . . . to count electrical pulses.



ASSEMBLY PROBLEMS, such as fixing hair-thin wires to barely visible germanium wafers, are solved by new tools and mechanized techniques. Finished transistors withstand great vibration and shock. Engineers see many opportunities for these rugged devices in national defense.



MOIST PAPER AND COIN generate enough current to drive audio oscillator using junction transistors. Half as big as a penny matchbox, an experimental two-stage transistor amplifier does the work of miniature-tube amplifiers ten times larger.

A tiny amplifying device first announced by Bell Telephone Laboratories in 1948 is about to appear as a versatile element in telephony.

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SEMI-CONDUCTORS: The electronics industry has, since its early days, been completely dependent upon the device which gave it life—the vacuum tube. The key of all electronics has been and is still the ability to control a greater power by a smaller power—a greater power in the form of an electric current flowing through a vacuum, by a much smaller power applied to control elements inside the vacuum.

Now, with justifiable confidence, I say that on the horizon are potential successors to vacuum tubes—devices with many advantages over vacuum tubes and but few disadvantages. These fantastic devices are called “diodes” and “transistors” and are made of Germanium. They are smaller, lighter, and potentially cheaper than their tube counterparts. They require no hot filament or hot cathode, hence require much less power to operate and, as far as we now know, have an indefinitely long life.

The properties of Germanium that make it valuable arise from the fact that it is a semiconductor—midway in its electrical properties between such metals as copper and such insulators as glass. More importantly, its ability to conduct electricity depends strongly on the amount and nature of its impurities. When one type of impurity is present in a layer of Germanium and another type in an adjacent layer of Germanium, current will only flow easily in one direction between the layers. This is useful in changing alternating current into direct current, so by analogy to the vacuum tube having similar properties, such a two-layer device is called a “diode.” It has been found within the past several years that when three layers of Germanium are used, the outer ones containing one type of impurity and the inner one another type of impurity, the two boundaries between the outer layers and the inner layer roughly correspond to the input and output circuits of a vacuum tube. That is, a small amount of control power applied to one boundary can influence greatly the flow of current across the other boundary and hence amplification can be achieved. Such a device is called a “transistor.” It has already been demonstrated that for almost every function a vacuum tube can fulfill there is a counterpart achievable by a “transistor.”

Diodes have been made in small sizes by the millions for several years now.

In one direction our scientists are seeking to make high-power or large “transistors”; in another direction they have already made them smaller than the head of a match. Several thousands of the small ones could be operated on the power required by one vacuum tube such as is used in your radio or TV set.

It is not difficult to extrapolate from here some of the implications for the future. A really *personal* radio of hearing aid size running indefinitely on one set of batteries is within sight. The giant digital computers or magic brains, which at present use several thousand vacuum tubes and occupy a large room, can conceivably become small enough, and incidentally reliable enough, to apply to every-day business and industrial problems as we now apply computers. In military electronics the simplicity and ruggedness of the transistor as well as its small size and low-power drain will have a direct effect on all equipment, particularly that which is airborne. In the telephone business it will become entirely practical to build amplifiers for use on cables at the bottom of the sea.

But what will happen to tubes? Will they disappear or become a ghost industry? Some kinds of tubes *certainly* will not, unless as yet undiscovered methods of using “transistors” are found. At present the frequency obtainable with “transistors” is definitely limited. This limit is high enough, however, so that most of the tubes used in radio and television are at least conceivably replaceable.

Lest you infer from what I have said that the tube industry, as such, is doomed, let me hasten to say that a prodigious amount of work remains to be done in the transistor field—work which is mainly research—before we can be certain that we can manufacture them with the same facility or in the same quantities that we now make vacuum tubes.

*New York Society of Security Analysts,
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Survey of Physiological Science

THE American Physiological Society indicated its interest in constructive planning by sponsoring two committee studies in 1945 and 1946. The reports showed the need and opportunity for a serious examination of the status and trends of physiological science. This year seemed propitious, and, with approval of the council, Ralph W. Gerard, chairman of one of the earlier committees and now president of the society, approached the National Science Foundation last fall for support. The foundation is concerned with like problems for all of science, and it responded enthusiastically. On April 4 Alan T. Waterman, director of the foundation, reported on this page:

At the present time we are discussing with a leading society a plan, proposed by the society itself, to review the present and potential research activities in its field, to survey its trained manpower resources, and to study the relationship of this field to science and education in general.

The foundation has subsequently announced the award of a contract to the American Physiological Society for a two-year study of the history, status, and role of physiology in the United States (SCIENCE, 115, 566 [1951]).

Founded in 1887 "to promote the advance of physiology," the American Physiological Society now represents 1310 professional physiologists from universities, industry, government laboratories, institutes, and foundations. Physiologists are interested broadly in functional processes of living organisms, and for this segment of science the society and the National Science Foundation are alike concerned with four main problems:

- 1) National and other policy for promoting research and education in physiology;
- 2) The impact of physiological science upon the national welfare, via medicine and related professions, agriculture and animal husbandry, industry, government, foundations, and universities;

3) Existing and projected resources (finances, installations, materials, persons) and programs of research and teaching in physiology by educational institutions, industry, and government;

4) The present status, past development, and projected trends of research content and practice and of teaching emphasis.

The Survey of Physiological Science is the first stocktaking endeavor to be supported by the National Science Foundation, and it is hoped that it will be a prototype from which similar efforts in other fields of science may benefit.

The central committee created to direct the two-year survey is under the chairmanship of Ralph W. Gerard, professor of physiology, University of Chicago. Deputy chairman is Wallace O. Fenn, professor of physiology, University of Rochester.

Ex officio members are Eugene M. Landis, president-elect of the society, and Milton O. Lee, executive secretary and managing editor. Orr E. Reynolds, on leave from the Office of Naval Research, where he is director of the Biological Sciences Division, is serving as executive director for the initial phase of the survey.

The success of such an investigation will depend upon the choice and range of problems studied, the methods of approach, and the critical and incisive evaluation of the findings. The collaboration of many individual scientists and societies having physiological interests will be sought. Especially helpful, however, is the sound background that advice from interested scientists can provide. Suggestions relative to physiological research, education, and administration; means of inquiry and scrutiny; and sources of collected information are solicited. The committee and staff will be grateful for all such suggestions, which may be addressed to:

Survey of Physiological Science
American Physiological Society
2101 Constitution Ave.
Washington 25, D. C.

RALPH W. GERARD
ORR E. REYNOLDS

The American Physiological Society

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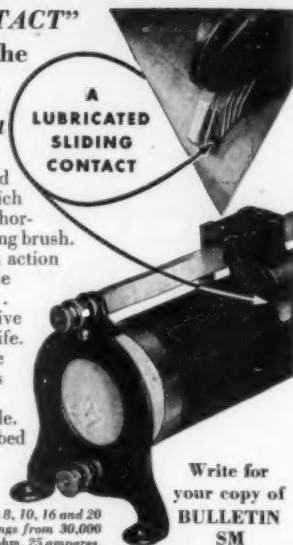
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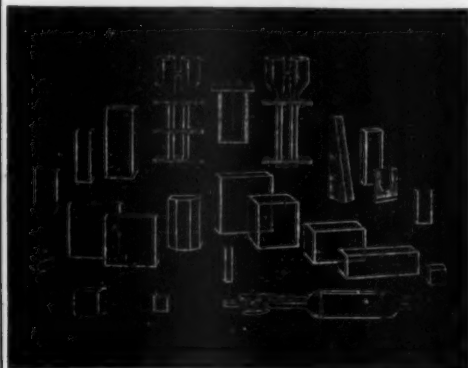
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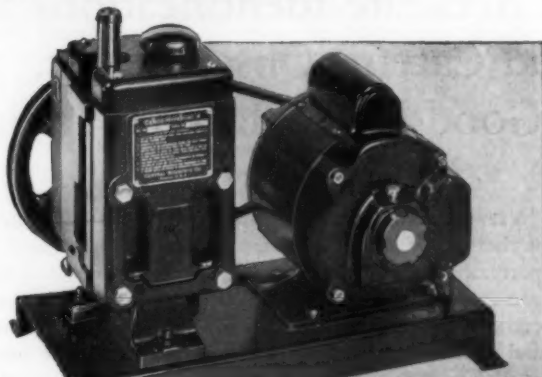
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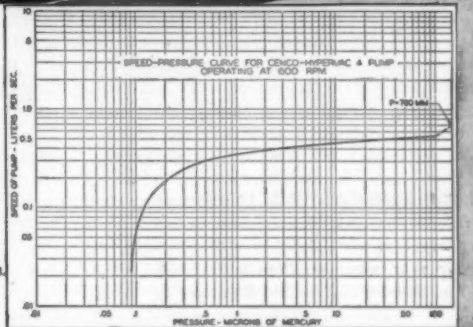
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Integrated Enzyme Activity in Soluble Extracts of Heart Muscle

D. E. Green

Institute for Enzyme Research, University of Wisconsin, Madison

THE CELLS OF PRACTICALLY ALL ANIMAL TISSUES contain a complex of enzymes, probably several hundred in number, which are so interdigitated structurally and functionally that the complex can be treated as if it were a single entity. The structural unit of this complex of enzymes has been identified as the mitochondrion (1-3), and the term "cyclophorase" has been applied to the functional or enzymatic activities exhibited by the constituent enzymes (4, 5). The cyclophorase-mitochondrial system catalyzes among other processes (a) the complete oxidation of members of the citric acid cycle, (b) the complete oxidation of fatty acids (6) and certain amino acids (7-9), (c) oxidative phosphorylation (10), and (d) various synthetic functions, such as the synthesis of hippuric acid (11) and citrulline (12). When mitochondria are prepared under proper conditions, they contain the full complement of enzymes and coenzymes necessary for bringing about each of the above-mentioned complicated series of reactions. One of the most fascinating problems of enzyme chemistry is that of elucidating the chemical organization that underlies the arrangement of the constituent mitochondrial enzymes, and recognizing the operational principles that underlie the reactions catalyzed by the complex.

Recently a nonmitochondrial system from pig heart has been reconstructed which catalyzes all the reactions characteristic of the organized complex (13). The heart system consists of three parts: a particulate nonmitochondrial fraction, a group of soluble enzymes, and a group of nucleotide coenzymes. The major components of the coenzyme group are di- and triphosphopyridine nucleotides (DPN and TPN), coenzyme A (CoA), and adenosinetriphosphate (ATP). The particulate fraction appears to supply mainly the enzymes necessary for interaction with molecular oxygen. When oxygen is replaced by some other suitable electron acceptor, many of the reactions carried out by the original heart system can now be duplicated with soluble enzymes in the presence of the necessary coenzymes. A measure of progress has been made in documenting the properties of some of these soluble enzymes. The rest of this article will be devoted to a consideration of some basic properties of the pyruvic and α -ketoglutaric oxidases, acyl coenzyme A deacylase, DPN cytochrome reductase, and the group of enzymes that collectively implement oxidative phosphorylation and the activation of acetate, acetoacetate, and fatty acids. Much of the complexity of

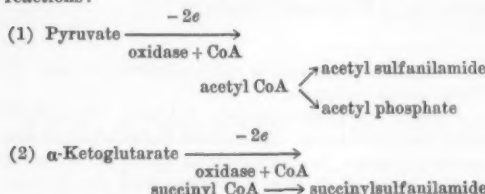
the mitochondrial unit is still mirrored in some of these soluble enzymes.

Pyruvic and α -ketoglutaric oxidases. Chronologically the discovery of the method for solubilizing the pyruvic oxidase by Jagannathan preceded all other studies referred to here. He found that the oxidase could be extracted by multiple freezing and thawing of the particulate fraction (microsomal) of pigeon breast muscle. The systematic exploration and isolation of this oxidase was undertaken by Jagannathan and Schweet (14). They have obtained the oxidase of pigeon breast muscle in homogenous form, as shown by Schweet *et al.* (15) in electrophoresis and ultracentrifuge studies. It has a molecular weight of about 4 million. The oxidase catalyzes (a) the oxidation of pyruvate to acetate and carbon dioxide; (b) the dismutation of diacetyl to acetoin, acetate, and carbon dioxide; and (c) the anaerobic conversion of pyruvate to acetoin and carbon dioxide. As isolated, the oxidase requires only the addition of co-carboxylase for activity, although in some preparations a partial requirement for magnesium ions is also demonstrable. The addition of no other coenzyme is needed for the oxidation of pyruvate to acetate when ferrieyanide or methylene blue is used as an electron acceptor.

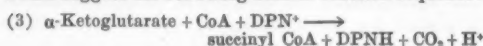
Subsequently Sanadi and Littlefield (16) isolated the α -ketoglutaric oxidase of pig heart muscle in homogenous form. The enzyme was also extracted from the particulate fraction by alternate freezing and thawing. The molecular weight of the oxidase is in the same range as that of the pyruvic oxidase of pigeon breast muscle—i.e., about 2 million. Two catalytic activities accompany the oxidase at all stages of purity: the oxidation of α -ketoglutarate to succinate and the anaerobic decarboxylation of α -ketoglutarate to succinialdehyde. No additional components are needed for the reaction of the α -ketoglutaric system with ferrieyanide or indophenol.

Jagannathan and Schweet (14) have been able to link the soluble pyruvic oxidase system of pigeon breast muscle with the sulfanilamide acetylation system of Lipmann (17) through CoA as the intermediary coenzyme. Under these conditions the net reaction is the oxidative acetylation of sulfanilamide by pyruvate. A similar link was effected by Sanadi and Littlefield between the α -ketoglutaric oxidase and the Lipmann acylation system, leading to the oxidative succinylation of sulfanilamide by α -ketoglutarate through CoA as the linking coenzyme (18). Other

acyl acceptor systems can be used in place of the Lipmann sulfanilamide acylase. Thus, Gergely and Hele (19) and Korkes *et al.* (20) linked pyruvic oxidase with the Stadtmann transacetylase (21) system of *Cl. Kluyverii* and accomplished the oxidative acetylation of inorganic phosphate by pyruvate. These observations point to the following formal sequence of reactions:

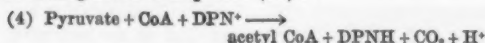


The fact that indophenol and ferricyanide can be used as electron acceptors in the assay systems for pyruvic and α -ketoglutaric oxidases, and that with these acceptors no additional cofactors are needed for maximal activity other than cocarboxylase and magnesium ions, has led to a good deal of confusion which has not yet been entirely cleared up. These two oxidases are also capable of interacting with DPN, and for this interaction CoA is an essential requirement, as was shown by the Ochoa group (20) and in our own laboratory (13). Sanadi and Littlefield (22) have now clarified the nexus between DPN reduction and CoA requirement. They have shown that, when CoA is added to the α -ketoglutaric oxidase system, as much DPN is reduced as CoA disappears. This would suggest the following formal reaction sequence:



Succinyl CoA has been identified by various diagnostic reactions (hydroxamic reaction, absence of mercaptan reaction, direct succinylation of sulfanilamide) and isolated from the reaction mixture in a relatively pure state. This represents the first unequivocal demonstration and isolation of an acyl coenzyme A compound formed as an intermediate in the oxidation of a keto acid. Such evidence could be interpreted to mean that both DPN and CoA are the prosthetic groups of α -ketoglutaric oxidase—the former acting as electron acceptor and the latter as succinyl acceptor.

When highly purified pyruvic oxidase free of lactic dehydrogenase is tested under the above conditions, a similar relation has been found between DPN reduction and CoA concentration; as expressed by the following reaction sequence (22):



Both the α -ketoglutaric and pyruvic oxidases require at least four prosthetic groups to catalyze the oxidative decarboxylation of their substrates: (1) diphosphothiamine, (2) magnesium ions,¹ (3) pyridine nucleotide, and (4) coenzyme A. The first and second

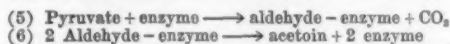
¹The requirement of the α -ketoglutaric oxidase for magnesium ions is as yet inconclusive.

are concerned with the decarboxylation of pyruvate or α -ketoglutarate to an intermediate at the aldehyde level. The third is concerned with the electron transfer by which the aldehyde intermediate is oxidized to the acyl CoA derivative, and the fourth is concerned with acyl transfer. Each of these components appears to be highly specific for its particular function. Diphosphothiamine is found bound to the respective enzymes, whereas DPN and CoA are usually completely dissociated.

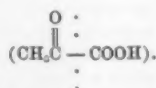
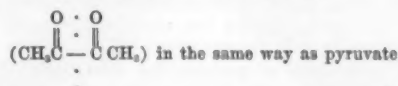
Recent studies by Gunsalus on the pyruvic oxidase systems of various bacteria have led to the discovery that the growth factor "protogen" is an essential constituent of these systems (23). The active principle has now been isolated by Reed *et al.* (24) in crystalline form and renamed α -lipoic acid. Considerable amounts of this factor have been found to be present in homogenous preparations of both the pyruvic and α -ketoglutaric oxidases of animal tissues. Thus a fifth prosthetic group, with function as yet unknown, has also to be brought into the complete picture for the pyruvic and α -ketoglutaric oxidases.

How can one explain the interaction of the α -ketoglutaric and pyruvic oxidases with indophenol or ferricyanide in absence of both CoA and DPN? There is the possibility that these oxidases contain in bound form a sufficient amount of both DPN and CoA to permit interaction at maximal velocity with ferricyanide or indophenol. However, analyses of the purified α -ketoglutaric or pyruvic oxidases have failed to disclose significant amounts either of DPN or CoA.

The isolation of the pyruvic oxidase in homogenous form has made possible the solution of two problems that have been shelved for some years. It has been known that animal tissues contain enzymes that catalyze the formation of one molecule of acetoin from two molecules of pyruvate (25), and the dismutation of diacetyl to acetoin, acetate, and CO_2 (26). Both these enzymatic activities have been found to be associated with the pyruvic oxidase of pigeon breast muscle from the first crude extracts to the stage of homogeneity. The mechanism of acetoin formation would appear to be as follows:



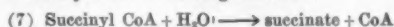
According to Schweet (27), the dismutation of diacetyl may be formulated as follows: diacetyl is cleaved at the carbon-carbon bond



That is to say, diacetyl is acted upon as if it were a substituted pyruvic acid. The cleavage of pyruvate yields an aldehyde enzyme product and CO_2 . The

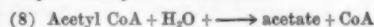
cleavage of diacetyl yields an aldehyde enzyme product and acetate. The former can undergo condensation to form acetoin, whereas the latter can be hydrolyzed to acetic acid. In line with this hypothesis is the observation that in the presence of ferri-cyanide, diacetyl is converted almost quantitatively to acetate, since the aldehyde enzyme product can be further oxidized to acetate. Thus the dismutation of diacetyl takes place only in the absence of an added electron acceptor.

Acyl coenzyme A deacylase. The purified α -ketoglutaric oxidase in the presence of substrate does not interact with DPN. Addition of a catalytic amount of CoA leads to no more reduction of DPN than is stoichiometric with the CoA added. Gergely, Hele, and Ramakrishnan (28) have found that when an extract of pig heart is added to the α -ketoglutaric oxidase system in the presence of catalytic amounts of CoA, DPN is rapidly and completely reduced. This extract contains an enzyme that has now been brought to a stage of high purity, and that has been shown to catalyze the following reaction:



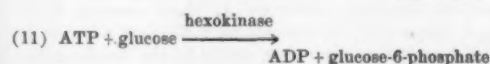
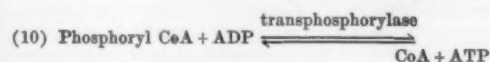
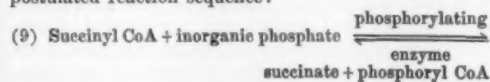
The enzyme thus has the character of an acyl CoA deacylase. Although the enzyme has been invaluable to the enzyme chemist in that it has facilitated the study of the interaction of the α -ketoglutaric oxidase with DPN, there is difficulty in understanding the physiological function of an enzyme that, in effect, nullifies the conservation of oxidative energy. Deacylase stands in the same relation to acyl CoA as ATP-ase does to ATP.

The presence of a second acyl coenzyme A deacylase specific for acetyl coenzyme A has also been demonstrated in crude extracts of pig heart (29). This enzyme catalyzes the reaction

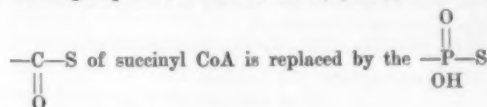


There are indications of the presence in heart extract of a deacylase that is active on acetoacetyl and β -keto-caproyl CoA (30).

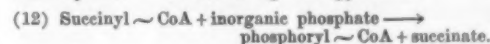
Oxidative phosphorylation. The purified α -ketoglutaric oxidase does not require inorganic phosphate, nor is the oxidation of α -ketoglutarate by suitable electron acceptors accompanied by the esterification of inorganic phosphate. However, when a soluble extract of pig heart muscle is added to the purified oxidase, the oxidation of α -ketoglutarate can now be coupled to esterification of inorganic phosphate (31, 13). The evidence is consistent with the following postulated reaction sequence:



The link with inorganic phosphate is brought about by an enzyme that catalyzes the replacement of a succinyl by a phosphoryl group. Assuming the functional group of CoA to be SH (Lynen), then the



of phosphoryl CoA. The high energy bond is conserved during the replacement reaction, as represented in the following formal equation, in which the Lipmann symbol \sim denotes a high energy bond:



The successful reconstruction of oxidative phosphorylation requires the separation of the phosphorylating enzyme from acyl coenzyme A deacylase. The latter decomposes succinyl CoA before the replacement reaction can take place and thus makes impossible the esterification of inorganic phosphate.

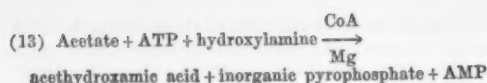
Kaufman, in Ochoa's laboratory (31), has attempted to reverse the above reaction sequence by starting with succinate and ATP in the presence of both the phosphorylating and transphosphorylating enzymes supplemented with CoA. The net reaction should be a CoA-dependent dephosphorylation of ATP to ADP and inorganic phosphate. Although this dephosphorylation does indeed proceed, the mechanism appears not to involve the reversal of Reactions (9) and (10).

The systematic purification and isolation of the enzymes involved in oxidative phosphorylation are being carried on in our laboratory by Sanadi and Littlefield (32). The application of low temperature alcohol fractionation has proved very useful as a means of separating them from acyl coenzyme A deacylase.

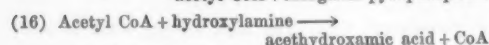
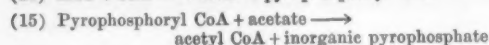
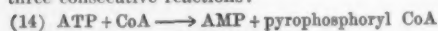
The system whose reaction sequence is represented in Equations (9) to (11) bears close analogies to its counterpart in the mitochondrial system. The oxidation process will come to a halt unless inorganic phosphate is present, since the deacylation of the oxidase is dependent upon replacement of the acyl group by inorganic phosphate. Furthermore, the oxidation leads to the formation of ATP, thus in effect converting oxidative energy into phosphate bond energy.

In the mitochondrial system, the oxidation of each member of the citric acid cycle, the oxidation of β -hydroxybutyrate and glutamate and the interaction of DPNH with flavin, and of reduced flavin with cytochrome are all linked with phosphate esterification. Much remains to be done on these different facets of the problem of oxidative phosphorylation. However, the experimental door is now slightly ajar and appears not too resistant to being opened further.

Activation of acetate. A soluble enzyme has been prepared from extracts of pig heart muscle in purified form which, in the presence of CoA and magnesium ions, catalyzes the following reaction (30):

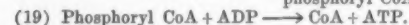
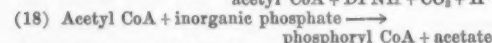
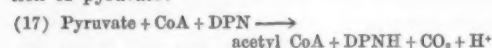


This over-all process presumably is brought about by three consecutive reactions:



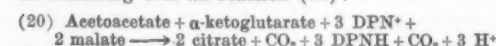
The enzyme that catalyzes Reaction (15) is active toward propionate but not butyrate. Sodium but not potassium ions inhibit the activity of this enzyme.

Inspection of Equations (14) and (15) discloses that the activation of acetate is not the reverse of oxidative phosphorylation accompanying the oxidation of pyruvate:

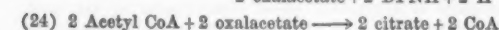
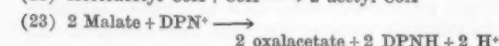
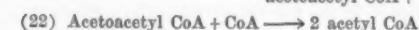


Acetyl CoA can be shown to be formed as the product of oxidation of pyruvate and of the interconversion of ATP, CoA, and acetate. The intermediary formation of phosphoryl CoA in the former case and of pyrophosphoryl CoA in the latter case has still to be established by direct isolation, although there is much supporting evidence for intermediaries.

Activation of acetoacetate. Soluble extracts of pig heart muscle contain enzymes which rapidly catalyze the following over-all reaction (30):



This appears to be made up of the following constituent reactions:

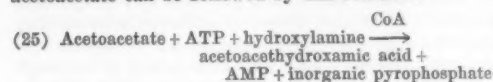


Acetoacetate can be replaced by other β -ketoacids such as β -ketovalerate and β -ketocaproate. The activity declines with increasing chain length and is essentially zero toward β -ketooctanoate.

Two simpler and more direct test systems have been devised for demonstrating the formation of acetoacetyl CoA. The breakdown of ATP (ADP) to ADP (AMP) and inorganic P can be catalyzed by small (catalytic) amounts of acetoacetate in the presence of the appropriate heart enzyme fraction. The reaction sequence involves the formation of acetoacetyl CoA and its breakdown by an acyl coenzyme A deacylase. A small amount of acetoacetate can thus bring about the dephosphorylation of a large amount of ATP. Other β -ketoacids such as β -ketovaleric and β -ketocaproic acids can replace acetoacetic acid. This

ATP-ase type of test system has also been useful in demonstrating acyl coenzyme A formation from acetic and propionic acids.

Under appropriate conditions the activation of acetoacetate can be followed by this reaction:



This has proved to be the simplest assay system for the activating enzyme.

Oxidation of fatty acids. Fatty acid oxidation as carried out in soluble extracts of pig heart may be resolved into three component processes (33): (1) the formation of the fatty acyl CoA compound starting with ATP, CoA, and fatty acid; (2) the β -oxidation of this compound to the corresponding β -ketoacid; and finally (3) the cleavage of the β -ketoacid CoA compound to acetyl CoA and an acyl CoA with 2 carbon atoms less than the parent fatty acid. There are at least three physiological mechanisms for forming the fatty acyl CoA compound. The first involves replacement of the pyrophosphoryl group in pyrophosphoryl CoA by a fatty acid. The second involves Reaction (22) in which the higher β -ketoacid is cleaved into acetyl CoA and fatty acyl CoA. The third involves a replacement of the succinyl group in succinyl CoA by a fatty acid—cf. Reaction (21).

A group of enzymes is involved in the activation, respectively, of fatty acids, α - β unsaturated acids, and β -hydroxyacids. Thus, one enzyme derived from pigeon liver and pig heart catalyzes the interaction of butyrate and caproate with hydroxylamine in the presence of ATP and CoA. Octanoate is acted upon relatively slowly by this enzyme. Crotonate and β -hydroxybutyrate are essentially inactive as substrates.

The enzymes concerned in the activation of fatty acids and in the disposal of β -ketoacids have posed no special technical difficulties. However, the enzymes concerned in the β -oxidation of activated fatty acids have proved to be exceptionally labile.

Role of coenzyme A. Considering the pivotal role of coenzyme A in practically all the important mitochondrial reaction sequences, it is appropriate to note that the recent advances in reconstructing mitochondrial activities in soluble extracts are mere extensions and applications of the fundamental studies of Lipmann (34) who, following his codiscovery of coenzyme A with Nachmansohn and Machado (35), worked out the operational principles of acyl transfer reactions. Many of the enzymatic mechanisms that have been considered in this article were anticipated and predicted by Lipmann, and a good deal of our contemporary terminology reflects the influence of his thinking. The elegant studies of fatty acid oxidation and syntheses in *Cl. Kluyverii* by Barker and Stadtmann (36) have also contributed greatly to our present knowledge of the mechanism of acyl transfer reactions involving coenzyme A. More recently Stern and Ochoa (37) have made an important advance in isolating the enzyme that catalyzes the condensation

of acetyl CoA and oxalacetic acid to form citric acid. Finally, Lynen (38) has pointed up the SH group of CoA as the group involved in acyl transfer reactions. These advances were all essential preliminaries to the successful reconstruction of oxidative phosphorylation and fatty acid oxidation in soluble extracts.

Consideration of any reaction sequence involving CoA reveals why it has been extremely difficult to resolve these sequences into a series of one-step reactions. For example, the activation of acetate involves the formation of pyrophosphoryl CoA and then a replacement reaction to form acetyl CoA. To study the latter reaction, pyrophosphoryl CoA must be provided as a substrate, whereas in the over-all reaction pyrophosphoryl CoA is acting catalytically. The substrates of a considerable number of enzymes are derivatives of CoA, and the only way these enzymes can be studied with reference to the particular reaction catalyzed is to supply the CoA derivative in substrate amounts. Until recently, it was not feasible to carry out such experiments. But with the development of a rapid and simple method by Beinert *et al.* (39) for isolating highly purified coenzyme A in good yield, the way is now open for the large-scale routine isolation of the biologically important derivatives of CoA, such as phosphoryl, acetyl, and succinyl CoA. The availability of these derivatives should make it possible to investigate one enzymatic reaction at a time.

The interdependence of reactions involving acyl transfer through CoA may help to clarify the necessity for an organized structure like the mitochondrion. It may well be that structural contiguity of enzymes makes for greater efficiency in executing reaction sequences in which activated molecules are transferred from one enzyme to another.

DPN cytochrome reductase. The interaction of DPNH with cytochrome *c* is a process that hitherto has been demonstrable only in particulate preparations. Edelhoch, Hayaishi, and Tepley (40) have solubilized DPN cytochrome reductase, starting with a particulate fraction of pigeon breast muscle. More recently Mahler, Vernon, and Sarkar (41) have achieved the same result with pig heart muscle and have succeeded in obtaining DPN cytochrome reductase in homogenous form.

There are two categories of enzymes involved in the oxidation of DPNH: (a) the diaphorases, which catalyze the oxidation of DPNH by various non-physiological electron acceptors; and (b) the reductases, which catalyze the oxidation of DPNH by cytochrome *c*. The relationship between these two types of enzymes has been obscure. Electrophoretic studies of cytochrome reductase have established that both diaphorase and reductase activities are associated with the same flavoprotein component. Diaphorase activity would thus appear to be a consequence of the partial inactivation of the reductase enzyme.

Cytochrome reductase is a flavoprotein with a molecular weight of about 70,000, based on spectrophotometric flavin analyses and physical measurements. The flavin prosthetic group is probably not identical either with flavin adenine dinucleotide or flavin monophosphate, though under certain conditions it can give rise to the latter.

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News and Notes

The Rochester Conference on Meson Physics

A SMALL informal conference on meson physics was held at the University of Rochester Jan. 11-12. Approximately fifty out-of-town guests, representing high energy physics laboratories throughout the country (and including several British physicists visiting the U. S.) attended the conference, in addition to the local staff. The first day of the conference, presided over by Enrico Fermi, was devoted to π meson interactions with nuclei, and the second day, presided over by J. Robert Oppenheimer, was spent discussing the new unstable particles. The conference, organized by R. E. Marshak, chairman of the Physics Department, was the second in a series made possible by the support of a group of Rochester industries.

During the first morning session, measurements of the interactions of accelerator-produced π mesons with complex nuclei were reported by Lederman (Columbia), Steinberger (Columbia), Bernardini (Illinois), Alvarez (Berkeley), and Anderson (Chicago). Piccioni (Brookhaven) and Salvini (Princeton) also presented results obtained with cosmic ray-produced π mesons. The accelerator results show a large reduction from the interaction cross section with free protons, which may be interpreted as indicating that the meson scattering amplitudes for protons and neutrons have opposite sign. Nuclear-coulomb scattering interference is clearly shown in the Columbia data, and, as Serber (Columbia) pointed out, there is also some indication of correlation scattering by individual nucleon pairs, in addition to the usual diffraction scattering by the nucleus as a whole. More striking is the observation of pairs of fast protons, consistent with the reaction $\pi^+ + d \rightarrow p + p$ in nuclear matter and, according to Bethe (Cornell), indicating the presence of approximately $5Z$ "deuterons" in the nucleus. In other words, in this experiment a complex nucleus does not appear structureless but exhibits strong correlations between the momenta of two nucleons at separations of 5×10^{-14} cm.

The afternoon session of the first day was opened by a report from Anderson on the measured absorption of π^+ and π^- mesons in hydrogen. Between 50 and 170 mev, the π^- cross section rises to a value of about $\pi(h/\mu c)^2 = 61$ mb (where μ is the π meson mass) and retains this value (or slightly less) at 217 mev. The π^+ absorption cross section rises rapidly from about 20 mb at 56 mev to 152 mb at 135 mev. A single crude measurement of the charge exchange (i.e., $\pi^+ + p \rightarrow \pi^0 + n$) and direct π^- differential scattering cross sections in the neighborhood of 90° and at an energy of 112 mev indicated that the former is twice as large as the latter. Assuming isotropy, comparison of this result with the π^+ scattering at this energy shows that the π^+ , π^- charge exchange, and direct π^- scattering cross sections are approximately in the ratio 9:2:1.

Fermi (Chicago) pointed out that these ratios would hold exactly if the isotopic spin were a good quantum number and scattering takes place only in the $T=3/2$ state (T is the total isotopic spin of the nucleon plus π -meson system). A more detailed explanation was given by Brueckner (Indiana) in terms of an isobaric resonance at 137 mev in the $T=3/2$, $J=3/2$ state (J is the total angular momentum), which he had already invoked to explain the photoproduction of neutral π mesons. Subsequent discussion made it clear that Brueckner's interpretation is by no means forced by the data. Wentzel (Chicago) next showed that orthodox strong coupling theory indicates the possibility of an isobaric resonance, although the quantitative predictions do not correspond to Brueckner's picture. Messiah (Rochester) mentioned certain critical tests of the charge independence hypothesis (constancy of the isotopic spin) in the form of π meson production experiments involving nuclei of known isotopic spin. The session ended with a report by Fermi on the electron contamination of the Chicago meson beam and by Coccoconi (Cornell) on the photoproduction of neutral mesons in hydrogen, deuterium, and carbon. Coccoconi finds that approximately equal numbers of neutral π mesons are produced from protons and neutrons, and that the cross section is not appreciably reduced in complex nuclei by the presence of other nucleons, in contrast to the experimental results for charged meson production.

The sessions during the second day were devoted to a critical survey of the present status of the new unstable particles. Firsthand reports of V -particle experiments were supplied by Fretter (Berkeley), Thompson (Indiana), and Rossi (MIT); and the results obtained by Leighton (CIT) and at Manchester were also discussed. There is general agreement that no single decay scheme will fit the data, although Leighton's interpretation of the neutral V -decay as leading to a proton and a π^- meson with two distinct decay energies of 34 ± 3 mev and 75 ± 5 mev is in disagreement with the Manchester analysis in terms of two types of particles $V_1^0 \rightarrow p + \pi^- + 46 \pm 6$ mev and $V_2^0 \rightarrow \pi^+ + \pi^- + 122 \pm 13$ mev. Leighton's data seem to exclude the possibility of a third (neutral) particle being emitted, and no investigator has found evidence for the electromagnetic component that would be associated with the emission and decay of a neutral π meson. Since in one MIT picture both decay products of the neutral V -particle produce nuclear interactions in lead, it is probable that μ mesons do not appear as decay products. George (Birkbeck) and Peierls (Birmingham) reported that the Bristol group has established the existence of two more unstable particles: $\tau^+ \rightarrow \pi^+ + \pi^+ + \pi^-$ and $\kappa \rightarrow e^+ + (\tau)2\nu$; however, recent evidence for the copious production of κ mesons in high energy "jets" is more questionable, since it depends on the exact nature of the increase of ionization with energy in the extreme relativistic region

(according to Ritson [Rochester]). Greisen (Cornell) also showed that the distribution in angle of μ mesons observed underground is inconsistent with their arising from the decay of κ mesons unless the κ lifetime is comparable to that of the π meson. Finally, Lord (Chicago) presented some data on V -tracks in photographic emulsions exposed to the high energy π meson beam from the Chicago cyclotron, which could be interpreted as due to V -particles, although this interpretation is hardly unique.

Oppenheimer (Institute for Advanced Study) opened the theoretical discussion of the new unstable particles by pointing out that the central problem is to reconcile the large production cross sections with the long decay lifetimes. Three categories of theories have been proposed which can be schematized as: (1) the "live parent," (2) the "heavy brother," and (3) selection rules. A "heavy brother" type of theory was proposed by Pais (Institute), who postulates a strong interaction, like the Yukawa interaction, that allows the new particles to be produced in pairs. The subsequent decay of each particle is then governed by a weak interaction (coupling constant of the order of 10^{-11}) not previously encountered in physics. Pais hopes ultimately to see a theory of three families of "elementary particles": (a) nucleons and heavy V -particles, (b) π mesons, light V -particles, and τ mesons, and (c) electrons, μ mesons, and κ mesons, which will not only predict their mass spectra but also the appropriate selection rules. Marshak closed the discussion by remarking that a selection rule type of theory seems adequate to explain the τ and κ mesons, but would be much more difficult to apply to the V -particles.

H. P. NOTES

*Department of Physics
University of Rochester*

Scientists in the News

Alfred L. Anderson, professor of economic geology at Cornell University, will make a detailed geologic examination for the Idaho Bureau of Mines and Geology of the fluor spar deposits of the Meyers Cove district. This will be a continuation of an investigation made by Dr. Anderson in 1942, shortly after the discovery of the deposits.

Jacques Benoit, of the University of Strasbourg, has been appointed head of the Service d'Histophysiologie, Station Physiologique du Collège de France, in Paris. This appointment will provide Professor Benoit with facilities to continue and expand his studies in the field of reproductive physiology.

Harrison C. Blankmeyer has been appointed director of the Owens-Corning Fiberglas Research and Development Laboratories to assist Games Slayter in coordinating product development and process improvement programs. From 1937 to 1951 he was employed by Joseph E. Seagram & Sons in Louisville,

and since early 1951 he has been assistant to the president of Kingan & Co., Indianapolis, where he established an industrial educational program in cooperation with Butler, Indiana, and Purdue universities.

Directors of the Eastman Kodak Company elected Albert K. Chapman president to succeed Thomas J. Hargrave, who became board chairman. Donald McMaster, vice president, was named to the new office of general manager. The elections reflected the expressed desire of Perley S. Wilcox to retire from the chairmanship of the board, a post held by him since 1945.

Lowell T. Coggeshall, dean of the University of Chicago Division of Biological Sciences and Frederick H. Rawson professor of medicine, has been elected president of the Chicago Society of Internal Medicine. Two other University of Chicago professors were elected to presidencies of Chicago medical associations: William E. Adams as president of the Chicago Surgical Society, and Arlington C. Krause as president of the Chicago Orthoptics Society.

The Cornell Board of Trustees has conferred emeritus rank on Peter Debye, Todd professor of chemistry. Dr. Debye will retire from teaching but will continue at Cornell in research. Dr. Debye won the Nobel Prize in chemistry in 1936 for work on the dielectric properties of liquids and on x-ray and electron diffraction of molecules.

Victor R. Gardner, formerly director of the Michigan Agricultural Experiment Station and head of the Department of Horticulture there for many years, is joining the staff of the Department of Horticulture, New Jersey Agricultural Experiment Station, Rutgers University, to advise on the over-all research program and to conduct research in the field of pomology. He is replacing L. Fredric Hough, who is on leave in Liberia, where he is establishing a breeding program under the Point IV program.

The Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, has named Martin G. Goldner director of medicine. Until recently he was chief of the medical services of the Veterans Administration Hospital in Brooklyn.

Mary Dare Haithecock has been elected president of the National Foundation of Reading. The foundation is composed of educators and medical authorities concerned with disabilities in reading and with increasing reading efficiency. Dr. Haithecock is professor of education at City College and a staff psychologist of the New York Eye and Ear Infirmary.

H. Gordon Hayes is retiring from Ohio State University to accept the position of professor of economics and chairman of the Department of Economics in the Graduate School at Tulane University. Professor Hayes is this year completing 32 years of service as professor of economics at Ohio State. Under the state retirement law he would have been subject

to retirement next year. In view of the opportunity to go to Tulane, where his appointment is for an indefinite period, he is retiring a year early.

Adolph Jacoby, director of the Bureau of Social Hygiene in New York City's Health Department, has retired after thirty-six years of service in the city's war against venereal disease.

Norman Lloyd Johnson, of University College, London, will be engaged in teaching and research in the Department of Mathematical Statistics, University of North Carolina, for the academic year 1952-53.

On Apr. 29, Jean de Lagarde, consul-general of France in New York, presented **Serge A. Korff**, professor of physics at New York University, with the insignia of Chevalier of the Legion of Honor, in recognition of his distinguished service in physics research, and cultural relations involving France and the U. S. Dr. Korff has worked extensively in the fields of cosmic ray neutrons and Geiger counters, and his early work on cosmic ray neutrons laid the foundation for use of cosmic radiocarbon as a dating tool for archaeology.

Norbert J. Kreidl, director of chemical research at Bausch & Lomb, and **Vincent M. Young**, head of the firm's glass plant, represented the United States at a meeting of the International Commission on Glass in London. The 36-man international commission consists of three representatives chosen by ceramic societies in each of 12 glass-making countries. While abroad Dr. Kreidl and Dr. Young are also visiting optical glass plants and laboratories in France, Germany, Austria, and Italy.

Jan B. Le Poole, director of the electron microscope department at the Technical University of Delft, visited the U. S. recently for a two weeks' series of conferences with American experts in the field of electron microscopy. In addition to his work at Delft University, Dr. Le Poole devotes part of his time to the Dutch Organization for Applied Scientific Research.

The first honorary degrees of Doctor of Technology to be awarded by the Hebrew Institute of Technology were presented to **Walter C. Lowdermilk**, soil conservation expert, who at present is acting as adviser to the Israeli government; **Lorenzo A. Richards**, chief physicist of the U. S. Salinity Laboratory at Riverside, Calif.; **Ben Lockspeiser**, executive director of the Department of Scientific and Industrial Research of Britain; and **Pierre François Donnel**, head of the Laboratoire Dauphinois Hydraulique in Grenoble, France. All had participated in a United Nations-sponsored symposium on desert research.

The Housing Research Foundation of Southwest Research Institute has appointed two additional technicians to its staff: **Tom McGovern**, of Madison, Wis., a former director of the National Association of Homebuilders, who has joined the foundation's home

office at Essar Ranch in Texas; and **Donald L. Hisey**, of Canton, Ohio, who will become the foundation's first field representative, covering Ohio, northern Pennsylvania, and northern New York. The foundation seeks to raise housing standards by awarding merchant builders its seal of approval if their projects conform to its high quality standards.

Edward Marks, of the Department of Geology, University of Texas, and the Bureau of Economic Geology at Austin, was recently appointed curator at the Paleontological Research Institution, Ithaca, N. Y.

Eugene R. Marzullo has been appointed medical director of St. John's Episcopal Hospital, Brooklyn. A specialist in internal medicine, he has been clinical professor of medicine at the State University of New York's College of Medicine in Brooklyn since 1940.

W. Kenneth Menke, of the Pittsburgh Coke and Chemical Company, has been elected to the new position of vice president in charge of chemicals. Before he joined the company Mr. Menke had been with the Monsanto Chemical Company for 17 years, most recently as director of the development department.

Ralph A. Morgen, director of the Engineering and Industrial Experiment Station of the University of Florida, has been appointed to the staff of the Division of Mathematical, Physical and Engineering Sciences of the National Science Foundation. He will be in charge of the foundation's research support program in the engineering sciences. Formerly a consulting chemical engineer, Dr. Morgen joined the faculty of the University of Florida in 1938.

W. W. Rankin, who will retire from Duke University's Mathematics Department after 26 years' service, was recently honored by the department at a dinner. **W. W. Elliott**, of the Mathematics Department, presided, and **John J. Gergen**, department chairman, spoke on Professor Rankin's contributions to the university. Professor Rankin, who joined the Duke faculty in 1926, is founder and director of Duke's Institute for Teachers of Mathematics.

Hillary Robinette, Jr., research director of Amalgamated Chemical Corporation since 1948, has opened his own offices in Ardmore, Pa., as chemical consultant to business and industry. He will continue as a consultant to Amalgamated, where he has instituted a comprehensive research program that has led to product improvement and new product development.

Herbert H. Schell has been elected president of the American Foundation for Tropical Medicine. Mr. Schell is president of Sidney Blumenthal & Co.

Friedrich Schwarz has been named director of mechanical and design engineering by Radiation Counter Laboratories, Inc., Skokie, Ill. For the past five years he has been employed by the U. S. government at various rocket installations in this country. Prior to World War II, he headed his own engineering firm,

Precision Electromechanical Engineering Company, in Frankfurt am Main, Germany.

James H. Steele, of Atlanta, has been appointed to serve for five years on the WHO Expert Advisory Panel on Zoonoses, which is concerned with the investigation and control of diseases of animals transmissible to man. Dr. Steele is chief of veterinary public health for the Communicable Disease Center, USPHS.

Aaron C. Waters, former professor of geology at Stanford University, and **Francis J. Pettijohn**, editor of the *Journal of Geology* since 1947, have been appointed full professors in the Geology Department, The Johns Hopkins University.

V. C. Williams has become director of chemical development, Mississippi River Fuel Corporation, St. Louis. Mr. Williams was formerly associate director of research, Central Research Laboratories, General Aniline and Film Corporation.

J. H. Wills, of the Pharmacology Branch of the Chemical Corps Medical Laboratories at the Army Chemical Center, has just returned from a two months' tour of Europe, where he has been observing the work done at several research installations.

Charles-Edward Amory Winslow has been awarded the Leon Bernard Foundation Medal and Prize of the World Health Organization for outstanding contributions to social medicine. Dr. Winslow, professor emeritus of public health medicine at Yale University, was one of the principal speakers at the opening of the technical discussions at the fifth assembly of WHO. His subject was "The Economic Value of Preventive Medicine."

Education

The central **Canadian Arctic** will be the locale of a research project this summer led by **Alexander B. Klotz**, entomologist, of City College, New York. The party, which is composed of graduate students and technical assistants from the universities of Toronto and Ottawa, will focus its investigation on conditions in the Arctic that allow the breeding of mosquitoes and similar pests in huge numbers. The group, which will be based at Churchill, will be aided by the Royal Canadian Air Force and Mounted Police.

The sixth workshop of the **Foundation for Integrated Education** will be held at the Oregon State College, Corvallis, June 23-28. **Henry Margenau**, Higgins professor of physics and natural philosophy at Yale, will serve as chairman, and **George A. Lundberg**, head of the Department of Sociology at the University of Washington, as co-chairman of the 1952 workshop, which will deal with the methodological background common to the sciences and the humanities. **F. L. Kunz**, vice president and executive officer of the foundation, will function as general secretary of the workshop, which follows the meeting of the Pacific Division of the AAAS. The foundation, of

which **Kirtley F. Mather** is president, sponsors a continuing service to institutions of higher learning, developing integrative concepts in science, philosophy, and education, based upon a program of research.

The **Harvard School of Public Health** has received a grant of \$10,000 from Mr. and Mrs. A. M. Sonnabend, of Boston, to be used for experiments under the direction of **Stanley J. Sarnoff**, in the treatment and clinical investigation of patients with heart disease, especially that resulting in acute lung edema. The work will be carried forward in the recently completed cardiac catheterization laboratories of the Children's Medical Center and Peter Bent Brigham Hospital.

An **Inter-American Seminar**, sponsored by the Organization of American States, International Labour Organization, the U. S. government, and the University of Maryland, will be held in College Park, Md., Aug. 2-Sept. 6. The seminar will consider the problems of vocational education and training and pre-university technical education in the American republics in the fields of agriculture, industry, business, and home economics. Previous seminars in the series have been held in Caracas, Rio de Janeiro, and Montevideo and were concerned with educational problems in general, illiteracy and adult education, and elementary education. The Division of Education, Department of Cultural Affairs, Pan American Union, Washington, D. C., will supply further information.

New York University has named **David Dodds Henry**, president of Wayne University, executive vice chancellor. Dr. Henry will have primary responsibility for the university's educational program. **Rufus D. Smith**, provost since 1934, will retire in July, and when Dr. Henry takes office in September the post will be discontinued. **Thomas Clark Pollock**, who has been acting provost during a leave of absence of Dr. Smith, will return to his position as dean of Washington Square College.

Stanford University has appointed **Peter Franken**, of Columbia University, and **Donald R. Yennie**, of the Institute for Advanced Study, to its Physics Department. **Hans Staub**, former faculty member and now director of the Institute of Physics at the University of Zurich, will return to the campus to teach during the summer quarter.

The latest report of the **University Grants Committee** of the United Kingdom gives the financial and enrollment statistics in British colleges and universities for the academic year 1949-50. Although the number of new students (24,331) decreased 495, or 2%, from the preceding year, total enrollment (85,421) registered an increase approximating 2%. Of this number, 62,199, or 72.8%, received scholarship aid, and higher education's increasing dependence on government support is shown by the fact that 63.9% of institutional income came from Parliamentary grants. In 1948-49 the percentage was 59.2. Of special interest in a report that reveals much of the structure and some of the recent progress in British

universities are increased registration of Commonwealth and foreign students; the high enrollment in science and technology (56.4% of the total); an 18% increase in gross income, much of it from government appropriations; and a 28% increase in budgetary appropriations for faculty salaries and retirement allowances.

Grants and Fellowships

The Arctic Institute of North America has approved 14 research projects for the year 1952. Awards supporting the research have been made with the financial cooperation of the Office of Naval Research. Among the studies will be the continuation of Project Snow Cornice, a glaciological study of the Seward-Malaspina Glacier system on the Alaskan-Canadian border. The Saskatchewan Glacier, Alberta, will be investigated by R. P. Sharp, of Caltech, and Maynard M. Miller will follow up the work that has been carried on every summer since 1948 by the American Geographical Society on the Juneau Ice Field.

The Oak Ridge Institute of Nuclear Studies, which administers the fellowship program for the Atomic Energy Commission, has extended more than 200 fellowships for 1952-53. These comprise 184 predoctoral—131 in the physical and 53 in the biological sciences—and 19 postdoctoral—8 in the physical sciences, 9 in the biological sciences, and 2 in medical sciences. This is the last major renewal of the AEC fellowships. The program is being discontinued in view of the establishment of the National Science Foundation's fellowship program, covering the same general area.

The Higgins Scientific Trust will distribute a million dollars in equal amounts to Columbia, Harvard, Princeton, and Yale for scientific education during 1952-53. The Columbia program will emphasize chemistry, engineering, geology, physics, and zoology; Harvard and Yale, medicine and chemistry; Princeton, biology, geology, and physics.

Bryn Mawr has awarded the Lillia Babbitt Hyde Honor Scholarships in Science to Elizabeth Dudgale, of Ashland, Va., Elizabeth A. Hall, of Pasadena, and Lois Marshall, of New York City. Two honorary awards were given to Anne Ipsen and Margaret Putney, and Toby Price, Barbara Troxell, and Elizabeth Warren received honorable mention.

National Research Council of Canada scholarships, totaling \$227,900 for 1952-53, include 18 special scholarships of \$1500 each for study abroad, to be held in the following universities: California, Cambridge, Chicago, Cornell, Edinburgh, Illinois, John Innes, London, North Carolina, and Oxford. Five postdoctorate fellowships of \$2500 each were granted for work at Cambridge, Dublin, London, and Oxford.

Sigma Delta Epsilon Graduate Women's Scientific Fraternity will award \$500 for the best research paper submitted by one of its members, published or accepted for publication in a scientific journal during Oct. 1, 1951-Sept. 30, 1952, or presented at any

regular session of any scientific society during that period. For further information, address the president, Elizabeth Mackay, Coulter Hall, Purdue University, Lafayette, Ind. The prize winner will be announced during the AAAS meeting in St. Louis next December.

The Wenner-Gren Foundation for Anthropological Research has awarded 33 grants-in-aid and fellowships totaling more than \$112,000. Among them was a grant to aid publication of the AAAS Section H Symposium on Prehistoric and Historic Asia: Transpacific Contacts with the New World, which was presented at the annual meeting last year in Philadelphia. This will appear as a Memoir of the Society for American Archaeology, which is defraying part of the costs of publication. Marian W. Smith is editor. Hans Bielenstein, of Sweden, will continue his research on Chinese internal migration and population change at the University of California, Berkeley; and Maharaia Winiata, a Maori scholar, will come to Stanford University from New Zealand to study methods and techniques used in investigating problems arising from culture contacts.

In the Laboratories

Allied Chemical and Dye Corporation has formed a Nitrogen Division to take over the manufacturing and related operations of the nitrogen and organic sections of the Solvay Process Division. The new unit will be headed by Hugo Riemer as president; M. F. Fogler and F. T. Techter will be executive vice presidents.

Dow Chemical Company has named R. H. Boundy director of research. His position as manager of the plastics department will be filled by C. B. Branch, present manager of the technical service and development department.

Interchemical Corporation has elected Norman S. Cassel vice president, succeeding A. E. Gessler, who becomes emeritus director of research and who will continue as a full-time consultant. Mr. Cassel will be in charge of the research laboratories in New York City. William J. Rothenich will succeed Mr. Cassel as divisional president of Interchemical's Textile Colors Division.

Recent additions to the staff of Arthur D. Little, Inc., are Kenneth Gibson, who has joined the Industrial Economics Group, and Louis Hand, of Thurston Manufacturing Company.

Parke, Davis & Co. has elected Leon A. Sweet vice president and director of research and W. R. Jeeves vice president and director of overseas operations.

Sterling-Winthrop Research Institute has appointed Arthur L. Beyler to head the new Endocrinology Laboratory. Emily D. Hemke, medical technologist, has been appointed to work with Dr. Beyler. Stanley O. Winthrop has joined the staff of the Chemistry Division.

Meetings and Elections

At the annual meeting of the **American Ceramic Society**, in Pittsburgh, the following officers were elected: president, W. Edward Cramer; president-elect, R. R. Danielson; vice presidents, H. B. DuBois, H. H. Holscher, and Victor C. Swicker; treasurer, Edwin M. Rupp.

At its annual meeting in Austin, Texas, the **American Society of Ichthyologists and Herpetologists** elected John Treadwell Nichols and Helen T. Gaige honorary presidents; Charles M. Bogert president; John Tee-Van, George P. Meade, and George A. Moore vice presidents; Coleman J. Goin treasurer; and Arnold B. Grobman secretary.

A **Conference on Research in Race Relations** will be held at the University of Chicago July 26-30 and will be open to persons engaged in research, policy-making, or social action in the field. The meeting is sponsored by the university's Committee on Education, Training and Research in Race Relations and the National Association of Intergroup Relations Officials, and is made possible by a grant from the Field Foundation. For further information write to Helen E. Amerman, 4901 S. Ellis Ave., Chicago 15.

At the annual meeting of the **Federation of American Societies for Experimental Biology**, held in New York City, Apr. 14-18, D. B. Dill, past president of the American Physiological Society, presided as chairman of the Joint Session on "World Food Problems," at which three papers were presented. Total attendance was 6450, and 149 sessions were held, including symposia and panel discussions arranged by the American Physiological Society, the American Society for Pharmacology and Experimental Therapeutics, the American Institute of Nutrition, and the American Association of Immunologists. The new constitution and bylaws, having been approved, went into effect on Apr. 17. A committee of one representative from each of the constituent societies, in addition to E. M. Landis, chairman, was created for maintaining liaison with the Canadian committee making plans for the 19th International Physiological Congress in Montreal next year. The 1953 meeting of the federation will be held in Chicago Apr. 6-10.

The **Industrial Research Institute, Inc.**, has elected Fred Olsen, of Olin Industries, president, and Allen Abrams vice president. C. G. Worthington was re-elected secretary-treasurer. L. B. Hitchcock and H. G. Vesper were elected new members of the board, to serve for three years. Theme of the annual meeting was "The Stimulation of Creative Thinking." The 1952 Medal of the institute, awarded for outstanding accomplishments in the management field of industrial research, was presented to Roy Newton, of Swift & Company.

The **Southern Psychiatric Association** named the following officers at its annual meeting in Pinehurst, N. C.: president-elect, W. L. Waldron; vice presi-

dents, C. C. Odom and John Trawick. Newdigate M. Owensby continues as secretary-treasurer, and Joseph E. Barrett, E. M. Robards, and Wilnot S. Littlejohn were re-elected to the Board of Regents. President of the association for 1952 is O. S. Hauk.

At its annual meeting the **Virginia Academy of Science** presented the J. Shelton Horsley Research Award to H. H. Gourley, of the University of Virginia Medical School, for his paper on "The Role of Adenosine Triphosphate in the Transport of Phosphate in the Human Erythrocyte." Allan T. Gwathmey was chosen president-elect, C. L. Miller secretary-treasurer emeritus, and Foley F. Smith, secretary-treasurer. Lloyd C. Bird was installed as president, succeeding Paul H. Patterson. Elected to the council were Walter S. Flory and Sidney S. Negus, AAAS press director.

Miscellaneous

The **American Society of Agricultural Engineers** awarded the John Deere Gold Medal to Ivan D. Wood, of Denver, and the Cyrus Hall McCormick Gold Medal to Charles J. Seranton, of La Porte, Ind., at its annual dinner in Kansas City, Mo. The medalists were selected by an awards jury consisting of the seven immediate past presidents of the society.

The **Department of Agriculture** has announced the start of work on Alaska's first pulp mill, which will involve an investment of \$45,000,000, largest industrial enterprise in Alaskan history. The mill, which will take two years to complete, is being installed by the Ketchikan Pulp Company, a new concern jointly controlled by the Puget Sound Pulp and Timber Co. and the American Viscose Co. Wood will come from the Tongass National Forest, which is under the administration of the Forest Service. All logging is to be done in accordance with good forest practices, salmon spawning streams and recreational and scenic features will be protected, and the mill has been so designed as to prevent pollution of tidal waters.

The **National Science Foundation** has awarded travel grants to 19 American biochemists to enable them to attend the second International Congress of Biochemistry in Paris July 21-27. In making the grants, the foundation was guided by the recommendations of an *ad hoc* committee appointed by the American Society of Biological Chemists and endorsed by the Biological Chemistry Division of the American Chemical Society.

Chemicals wanted by the **Registry of Rare Chemicals**, 35 W. 33rd St., Chicago 16, Ill., include: Calcium thiocacetate; *n*-methyl synephrine; methadren; D-threitol; aneurine pyrophosphoric acid; cadaverine; 2-carbethoxythio-1-methylgloxaline; cysteine sulfone; coronene; guanazole; 2-mercaptobenzothiazole; 2,4-di-tert-butylphenol; 2,3,4-trihydroxy benzene-1-carboxylic acid; 9-acetylphenanthrene; 3-cyanopyrene; decanesulfonic acid; pentamethylene bromohydrin; glyoxalic acid; 3,4-xylydine; and dilithium amide.

Technical Papers

Thermal Stimulation of Isolated Organs and its Inhibition by Pharmacological Agents

N. Ercoli and Vittorio Guzzon

Istituto Sieroterapico Milanese Serafino Belfanti,
Milano, Italy

The effect of temperature variations on biological systems has been examined from various standpoints: sensitivity of isolated organs to drugs (1-3), thermodynamics of muscle contraction (4), biochemical changes (5), and reaction of the organism *in toto* (6-10). We investigated the effect of controlled temperature variations on the isolated intestine with the anticipation that this might give some clue to the mechanism of the thermal effect on the organism, especially so far as the possible intervention of a mediator is concerned. In exploring this possibility, we searched to obtain an inhibition of the thermal effect by pharmacological agents. About 150 experiments carried out so far permit a certain number of conclusions which we consider it worth while to report, while our *in vivo* studies are progressing.

Isolated intestinal strips were suspended, and recorded kymographically, in a Ringer solution containing, per liter: 9 g NaCl, 0.25 g KCl, 0.25 g CaCl_2 , 0.5 g glucose, and 0.5 g NaHCO_3 .

Care was taken to avoid exposure of the organs to uncontrolled cooling by collecting and suspending the strip as rapidly as possible from the guinea pig or rabbit just sacrificed, or by making the autopsy in a thermostatic chamber at 38°. The required temperature variation on the suspended strip was obtained by adding to the external water bath ice water or water at a temperature above 38°. The internal temperature of the glass tube containing the organ was continuously recorded.

Our findings regarding cold contractions were:

1) A sudden decrease of the temperature—for instance, from 37° to 24° C—induces a contraction of

the isolated guinea pig intestine. This contraction, which resembles those induced by histamine and acetylcholine, has a broader (more prolonged) shape than the latter, however. The fall of temperature which in all cases gave a typical cold contraction occurred at the rate of 10°/min. The deeper and more rapid the temperature fall, the more constant and typical is the outcome of the experiment.

2) It is possible to lower the temperature of the isolated guinea pig intestine to +4° without obtaining a cold contraction, if the temperature is decreased gradually (e.g., at a rate of 1° C/min).

3) The cold contraction is inhibited by synthetic antihistaminics (Benadryl, Pyribenzamine, Thienylpyramine) and by spasmolytic drugs such as Trasentine and Pavatrine, but it is not influenced by atropine. For example, Benadryl 1:200,000-1:400,000 inhibited completely the cold contraction (Fig. 1); atropine concentrations as high as 1:20,000 were ineffective.

4) The isolated guinea pig intestine conserves its sensitivity to histamine and acetylcholine until the temperature reaches +8°-10°. Its sensitivity to histamine and BaCl_2 becomes nil, or almost, at about +4°, whereas that to acetylcholine is still maintained at this low temperature.

5) When the temperature of the cooled guinea pig intestine is raised again to 37°, it reacquires its usual behavior and sensitivity not only to biochemical (ACH, histamine) stimulators, but also to another thermal (cold or heat) stimulation. In fact, in our experiments with intermittent temperature changes, the thermal contraction has been obtained repeatedly over periods of 4-8 hr.

6) At low temperatures (+4°) the contraction curve caused by acetylcholine and histamine, whenever it occurs, is greatly prolonged; the muscular contraction has a tendency to become spastic.

In contrast to the guinea pig intestine, that of the rabbit gives only a very short contraction, if any,

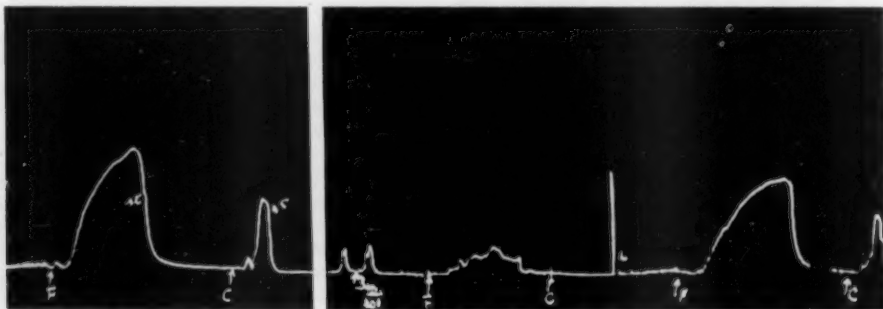


FIG. 1. Guinea pig intestine: F, cold contraction caused by sudden decrease from 38° to 4°, is followed by heat contraction (C) after bringing the temperature back to 38°. F and C are inhibited by 1:400,000 Benadryl. After washing with Ringer's (L) the initial thermal effect reappears.

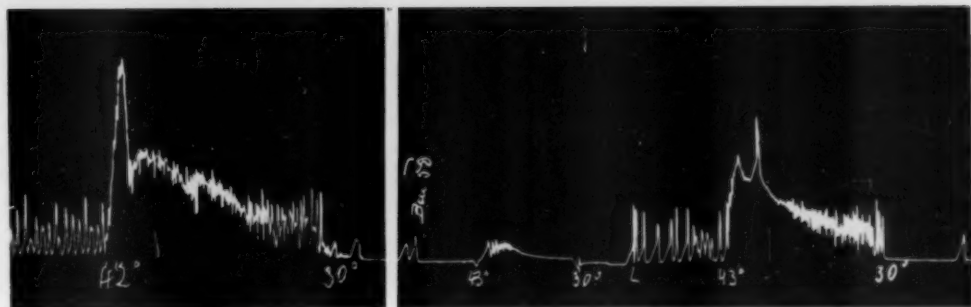


FIG. 2. "42°" heat contraction obtained by raising the temperature from 30° to 42°; "30°" intestine has been brought back to 30° C. Benadryl 1:50,000 inhibits the heat effect. After washing (L) the heat effect reappears.

upon lowering the temperature. Furthermore, at low temperatures (+4°) it loses its spontaneous contraction and its sensitivity to acetylcholine, epinephrine (1:100,000,000), histamine. When the temperature is brought back to the physiological zone (37°), the rabbit intestine reacquires its spontaneous contractions and its original sensitivity to the above reagents.

Regarding heat contractions, our findings were:

1) A sudden increase of temperature gives a contraction of the isolated guinea pig intestine, which characteristically can be obtained without surpassing the body temperature (e.g., by an increase from 25° to 37°). However, the contraction is more intense if the final temperature is above 35° (e.g., from 30° to 43°). The heat contraction occurs less regularly than that induced by cold; in our experience it has been obtained in about 60% of the trials.

2) The form of the heat-contraction curve is different from that obtained by temperature decrease; it is generally represented by a higher initial peak, followed in most cases by a number of rapid contractions, as illustrated in Fig. 2.

3) The heat contraction is greatly diminished or completely abolished by Benadryl, Trasentine, and Pavatrine and is not influenced by atropine. The initial peak contraction is more sensitive to the effect of these drugs than the more prolonged and lower part of the contraction curve. Thus, in favorable experimental conditions, it is possible to inhibit the first, higher contraction and to maintain the successive ones.

4) A certain differentiation between cold and heat stimulation is given by the behavior of the rabbit intestine, which reacts only to the latter. The heat contraction of rabbit intestine is inhibited by Benadryl.

Sudden temperature variations induce contractions of the isolated intestine which resemble those determined by chemical stimulators (acetylcholine, histamine, BaCl_2).

The duration of the cold-contraction curve is more prolonged than that obtained with chemical stimulators at physiological temperatures. The prolonged shape of the curve depends probably on the final temperature condition of the experiment rather than on the nature of the stimulus, since at low tempera-

tures histamine and acetylcholine also induce a more prolonged contraction of the guinea pig intestine. A decreased activity of the enzymes responsible for the destruction of the stimulators (histaminase, cholinesterase), determined by the drop of temperature, could account for the prolonged effect of the stimulation.

The responsiveness of the rabbit intestine to heat but not to cold stimulation can be related to the insensitivity of this organ to chemical stimulators at low temperatures.

Thermal stimulation depends on the rate of the temperature variation (i.e., on the variation of the energy content) and is independent of the absolute temperature reached. Thus, low (4°) as well as high (42°-44°) temperatures can be reached without contraction, by changing the temperature gradually.

The contraction induced by thermal stimulation is inhibited by the antihistaminics Benadryl, Pyribenzamine, and Thenylpyramine, and by the antispasmodic agents Pavatrine and Trasentine.

On the isolated intestine, Benadryl (benzhydrol-ether of dimethylaminoethane) possesses general antispasmodic properties, since it is effective against acetylcholine, histamine, and BaCl_2 , whereas the ethylenediamine derivatives (Pyribenzamine, Thenylpyramine) have activity mainly against histamine (11, 12).¹ The inhibiting effect of the latter drugs on the thermal contraction leads to the conclusion that antihistaminic activity is a sufficient condition to bring about inhibition. As a corollary, it may be assumed that histamine is the mediator responsible for the effect of thermal stimulation. In confirmation of this assumption atropine, the most effective antagonist of the acetylcholine effect on the guinea pig intestine, does not inhibit thermal contraction. The antithermal activity of Pavatrine and Trasentine might be attributed to their depressant action on the muscular fiber.

Direct transfer experiments, using the tissue-bath fluid after contraction, have not so far revealed (biologically) detectable amounts of any mediator. This, however, could depend on a rapid enzymatic destruction, on an intracellular liberation and fixation, or

¹ A correspondingly wider range of activity has been observed also *in vivo* for Benadryl (13). This drug, in contrast to the ethylenediamine antihistaminics, has a high protective action against the lethal cholinergic shock of guinea pig.

on minute amounts of the mediator liberated, etc.

There might be some relation between the role of histamine as a mediator of thermal stimulation and the increased histamine content in the perfusion liquid of isolated cat liver heated above 38°, reported by Rawlinson and Kellaway as an effect of cellular injury (5).

The experimental conditions described represent a convenient method of studying the influence of temperature variations on a reactive biological system, particularly from the standpoint of drug effect. Sudden temperature changes represent a stimulus for the smooth muscle, which contracts, probably as a result of the liberation of a histaminelike mediator. The contraction is inhibited by antihistaminic and antispasmodic drugs, but not by atropine.

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Effects of an Exogenous Growth Regulator on Proteolytic Enzymes of the Soybean Plant^{1,2}

S. R. Freiberg

Department of Plant Physiology,
Rutgers University, New Brunswick, New Jersey

In recent years it has been shown that 2,4-dichlorophenoxyacetic acid (2,4-D) decreases the amount of protein nitrogen in the leaves and increases the level of this fraction in the stems and roots of treated plants (1-6). Accordingly, it was considered possible that this growth regulator affects proteolytic enzymes differently in the leaves and in the stems and roots. To test this hypothesis soybean plants were treated with 2,4-D and analyzed for proteinase and polypeptidase activity in leaves, stems, and roots.

Plants were grown in solution culture until they were 38-40 cm tall and had 6 fully expanded trifoliate leaves. At that stage the soybeans were treated by

¹ Journal Series paper of the New Jersey Agricultural Experiment Station, Rutgers University, the State University of New Jersey, Department of Plant Physiology.

² This paper is based upon work done for the Biological Department, Chemical Corps, Camp Detrick, Frederick, Md., under Contract No. DA-18-064-CML-450 with Rutgers University.

TABLE 1
EFFECT OF 2,4-D ON PROTEINASE AND POLYPEPTIDASE ACTIVITY IN LEAVES, STEMS, AND ROOTS OF SOYBEAN PLANTS

Days after treatment	Leaves		Stems		Roots	
	Controls	Treated	Controls	Treated	Controls	Treated
<i>Proteinase Activity*</i>						
0	1.97	—	0.14	—	0.43	—
1	1.88	1.48	.10	0.19	.59	1.01
3	1.68	1.47	.04	.52	0.42	1.28
5	1.82	1.22	0.09	0.34	—	—
<i>Polypeptidase Activity*</i>						
0	2.55	—	0.77	—	0.86	—
1	—	—	.84	0.90	1.16	1.25
3	2.49	2.35	.66	0.79	0.81	1.65
5	2.35	1.55	0.75	1.10	—	—

* Measured as ml 0.05 N NaOH required to neutralize the increase in carboxyl groups after 24 hr incubation of plant enzyme extract with substrate of gelatin for proteinase activity or peptone for polypeptidase activity.

placing them in nutrient solutions containing 5 ppm of 2,4-D for an exposure period of 24 hr, after which the treated plants were returned to fresh nutrient solutions containing no 2,4-D.

Within 6 hr of the start of exposure to 2,4-D, twisting of stem tips and epinasty of petioles of treated plants were observed. By the third day after treatment, these symptoms were more pronounced, although all leaves were still completely turgid. By the fifth day, some of the leaves of the treated plants had wilted permanently and were just starting to turn dry. Most of the leaf tissue was still not dehydrated or dead, as indicated by the fact that the average percentage dry matter of all leaves of treated plants at this stage had reached only 19.5% as compared with 17.3% for the controls. Stems and bases of petioles of treated plants were definitely enlarged by this time.

Plants harvested before and after treatment were separated into the tissue fractions indicated in Table 1 and dried at 45° C. At each harvest reported in Table 1 all the leaves from 9 plants were composited into one sample for analysis. Each stem and root sample also represented all the respective tissue fraction from 9 plants. Glycerol extracts of the dried tissue were used for measurement of proteinase and polypeptidase activity according to methods described by Blagowestschenski and Melamed (7), Lauffer *et al.* (8), and Moundfield (9). Duplicate aliquots were analyzed, and determinations were repeated when good agreement between replicates was not obtained.

The results shown in Table 1 indicate that, with 2,4-D treatment, proteinase and polypeptidase activity decreased in the leaves by the end of the experiment, whereas in the stems and roots the activity increased considerably. The magnitude of the changes in proteolytic enzyme activity following treatment with 2,4-D indicates a significant influence of the growth regulator on this phase of nitrogen metabo-

lism. Obviously the activity of these two enzyme systems was not influenced by 2,4-D in the direction that might have been anticipated from observed changes in distribution of protein in leaves, stems, and roots following treatment of plants with 2,4-D (2). Possible interpretation of these findings will be presented elsewhere with further analyses of these plants.

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Chlorogenic Acid a Possible Metabolite in the Terminal Oxidase System of the White Potato¹

Gestur Johnson

Colorado Agricultural Experiment Station,
Fort Collins, Colorado

Since chlorogenic acid occurs in a significant amount in the white potato (*Solanum tuberosum*), it may be involved in other functions aside from the protective action against invasion by *Streptomyces scabies* and other types of injury as reported by Johnson and Schaal (1). Boswell and Whiting (2) were among the first to demonstrate experimentally that polyphenolase is involved in the respiration of the potato tuber. They were able to concentrate a natural tyrosinase substrate from potato tuber. This substance gave a green color with FeCl_3 which is characteristic of ortho-dihydroxy phenols. Upon adding it to respiring potato slices, they found increased rates of oxygen uptake and of carbon dioxide evolution. They were, however, not able to identify this substance. On the basis of the work of Johnson and Schaal, the indications are that it is chlorogenic acid.

Robinson and Nelson (3) contend that the active principle in potato juice which increases respiration is tyrosine. According to their view, tyrosine is oxidized to 3,4-dihydroxyphenylalanine (DOPA), which is the respiratory carrier. They estimated that 85% or more of the oxygen uptake may pass through this system.

The presence of chlorogenic acid in potatoes has been demonstrated by use of paper chromatography (1). However, no DOPA could be detected in potatoes by this method. Minute quantities of DOPA can be detected on a paper chromatogram by the use of Folin-Denis reagent or Pauly reagent (diazotized sul-

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fanilic acid). The former gives a blue, and the latter a reddish-brown, color with DOPA. These reagents failed to show any DOPA in concentrated extracts prepared from potato flesh.

Rudskin and Nelson (4) found the natural polyphenolase substrate in the sweet potato (*Ipomoea batatas*) to be chlorogenic acid, and they concluded that chlorogenic acid and polyphenolase are involved in the terminal oxidase system of the sweet potato.

In view of the fact that chlorogenic acid is a natural substrate for tyrosinase (polyphenolase), and is present in greater quantities in the potato than DOPA, the author suggests that chlorogenic acid rather than DOPA is involved in the terminal oxidase system of the white potato.

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Repeated Semiannual Spawning of Northern Oysters

V. L. Loosanoff and H. C. Davis

U. S. Fish and Wildlife Service, Milford, Connecticut

In Long Island Sound, as well as in ecologically similar areas, the spawning season of oysters, *Crassostrea virginica*, is confined to the period extending approximately from the last week of June until the beginning or middle of September. Thus the season is comparatively short and occurs once a year. It is the latter circumstance that suggested studies designed to determine whether the gonad development and spawning of the oysters were of the exogenous type—initiated and regulated by periodical seasonal changes of environment—or of the endogenous type—controlled by a pattern confined within the organism itself.

The question has been answered in part by experiments which showed that ripening of gonads in oysters could be achieved even in midwinter by placing the oysters for several weeks in warm water of about 20° C (1). It still remained uncertain, however, that this was not merely a case of precocious development of gonads which would make the oysters unable to undergo normal gametogenesis the following summer. To settle this an experiment was devised to find whether the oysters are able, under certain conditions, to accumulate and discharge spawn in a normal way at least twice a year, at intervals of about six months, and to do so for two or three successive years.

The experiment began in the spring of 1947 when a group of approximately 250 adult, individually numbered oysters was suspended on a float in Milford Harbor, Connecticut. By the middle of June, when the oysters reached ripeness, they were brought

into the laboratory and induced to spawn. After spawning they were returned to the harbor. Samples of the gonads taken approximately once a month for histological studies showed that by the middle of September the oysters had almost recovered from the summer spawning.

Toward the end of November the oysters began to hibernate. Late in December 1947 they were brought from the harbor, which at that time was covered with a layer of ice, and placed in the laboratory in running sea water at a temperature of about 4° C. Using our method for conditioning mollusks for winter spawning (2), the temperature was gradually increased a few degrees every two or three days until it was slightly over 20° C, after which the oyster became ripe within three to four weeks. They were induced to spawn in January and February 1948, discharging normal gametes.

Following spawning, and partial recovery of the oysters, the temperature of the water was gradually decreased. This process resembled fundamentally the condition occurring in our natural waters in late summer and fall. In March 1948 the oysters were returned to Milford Harbor, where the water temperature was only about 4° C—i.e., cold enough to make them hibernate.

Some of the oysters were returned to the harbor while their gonads were still in the process of active resorption and while they contained undischarged eggs. When examined early in May, at which time the water temperature was still below 10° C, the oysters remained in about the same condition. Apparently the temperature between the dates of return to the harbor in March and the examination was too low to permit active resorption of the remaining gonad material. However, with the increase of temperature, which reached 16° C by the end of May, the resorption proceeded more rapidly, and was soon completed.

Between the end of May and the middle of June 1948 the oysters again underwent and completed gametogenesis and were easily induced to spawn when brought into the laboratory. After the spawning they were once more returned to the harbor and went through the normal process of gonad resorption and glycogen accumulation, eventually entering hibernation late in the fall. Thus the condition and behavior of the oysters in the summer and fall of 1948 were basically the same as during the corresponding period the previous year, regardless of their unusual extra reproductive activities during the winter.

In January 1949 the oysters were again brought into the laboratory, conditioned, and induced to spawn. Then, following the procedure described for the preceding year, they were once more returned to the harbor. They again spawned in the summer of 1949. Thus within a period of two years, June 1947–June 1949, the oysters were made to develop gonads and discharge normal spawn on five occasions at approximately six-month intervals.

The experiments have shown that the processes of

gonad development and spawning of these oysters are not of the endogenous type; i.e., there is nothing in their physical pattern that will not permit reproduction oftener than once a year, provided the ecological conditions are favorable for all aspects of the physiological activities involved in this complex process.

The experiments have also demonstrated that the oysters, in developing gonads, showed no dependency on seasonal changes in such factors as light, tidal rhythm, precipitation, small variations in salinity, or other changes that usually occur during the spring and early summer when the gonads of oysters are rapidly developing. It has also been shown that gonad development of oysters is not dependent on certain types of plankton organisms that are present in the water only during the spring and summer, the time of normal gametogenesis and spawning.

Although the observations reported here concern oysters only, we think, nevertheless, that the conclusions may also apply to some other lamellibranchs. For example, in our work with the clam *Venus mercenaria*, several individuals have been spawned in the January–July–January pattern. This ability of some Northern lamellibranchs to be conditioned for spawning at more frequent intervals than under natural conditions offers an interesting and practical method for studies of physiological ecology, genetics, and other aspects of their behavior.

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Enzymatic Reduction of Cystine by Coenzyme I (DPNH)^{1,2}

Walter J. Nickerson and Antonio H. Romano³

Department of Microbiology, New Jersey Agricultural Experiment Station, Rutgers University, New Brunswick

The occurrence of glutathione reductase, catalyzing the reduction of oxidized glutathione (GSSG) by reduced triphosphopyridine nucleotide (TPNH), has been demonstrated in pea seeds by Mapson and Goddard (1) and in wheat germ by Conn and Vennesland (2,3). The latter authors (3) stated that their purified preparations of glutathione reductase are without activity toward cystine. Meldrum and Tarr (4) had previously supplied considerable circumstantial evidence for the occurrence, in rat blood and in yeast, of an enzymatic process utilizing TPNH for the reduction of GSSG. The property of reducing cystine has, for a long time, been attributed to plant and ani-

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³ Standard Brands Research Fellow in Microbiology.

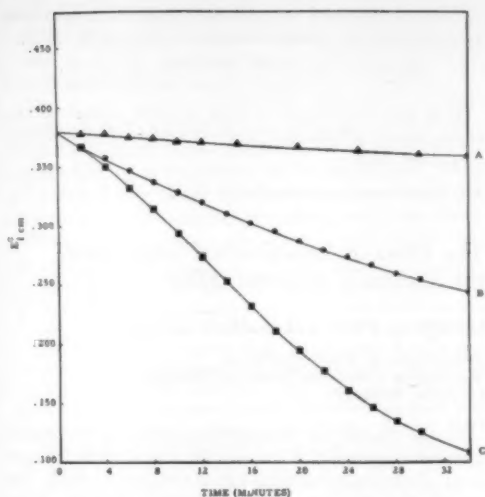
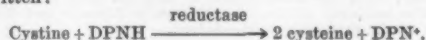


FIG. 1. Rate of oxidation of DPNH by a heat-labile cystine reductase system: Curve A, 1 ml heated cell-free extract of baker's yeast (in $M/40$ phosphate buffer, pH 6.2) + 1 ml DPNH solution (280 μ g) + 1 ml saturated cystine solution in $M/40$ phosphate buffer; Curve B, 1 ml cell-free extract of baker's yeast + 1 ml DPNH solution (280 μ g) + 1 ml buffer; Curve C, 1 ml cell-free extract of baker's yeast + 1 ml DPNH solution (280 μ g) + 1 ml saturated cystine solution in buffer.

mal tissues, but the mechanism of this reduction has not been elucidated. Tunncliffe (5) reported the existence, in tissue residues, of a thermostable substance capable of reducing disulfides. The statements of Abderhalden and Wertheimer (6) that frog muscle can be washed until it shows no power of reducing cystine, and that the reducing power can be restored by the addition of "Kochsafft" suggest the participation of a thermostable coenzyme.

After grinding washed cells of baker's yeast (starch-free pound cakes of Fleischmann's yeast) at 2° with powdered glass in a microhomogenizer designed by Brendler (7) (employing a Lucite rotor and made by E. Machlett & Son), we have succeeded in obtaining a cell-free extract containing a heat-labile enzyme catalyzing the reduction of cystine to cysteine by reduced disphosphopyridine nucleotide (DPNH). The rate of oxidation of DPNH in the presence of cystine and the enzyme (which may be termed *cystine reductase*) has been followed in a Beckman Model DU Quartz Spectrophotometer at 340 $m\mu$. The DPN (Schwarz Laboratories, 65% pure, TPN-free) was reduced by the method of Hogeboom and Barry (8). As shown in Fig. 1, a slow rate of oxidation of DPNH in the absence of cystine is occasioned by substances contained in the enzyme preparation; in the presence of cystine the rate of oxidation of DPNH is greatly accelerated. Heating at 100° C for 10 min completely destroys this activity. The apparent reaction may be written:



Reduced coenzyme II (TPNH) is without activity in this system. We have, however, observed glutathione reductase activity in cell-free extracts from baker's yeast; and, confirming observations of others (1-3), find that TPNH is the hydrogen-donating agent whereas DPNH is not active in the glutathione reductase system.⁴

The appearance of $-SH$ from the enzymatic reduction of cystine has been followed by iodine titration and by the phospho-18-tungstic acid method of Shinohara (9); the data obtained by the two methods showed excellent agreement. Cystine reductase activity has been found in acetone powder preparations of ungerminated peas (Topper variety) and in two strains of the pathogenic yeast *Candida albicans*, as well as in baker's yeast.

If acetone powder preparations of baker's yeast are washed, the ability to reduce cystine to cysteine is lost. This activity is restored to the washed residue by the addition of DPNH, as is shown in Fig. 2.

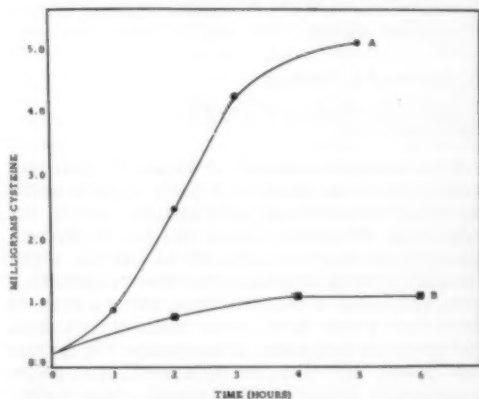


FIG. 2. Effect of DPNH on cystine reduction as measured by iodine titration: Curve A, 2 g washed acetone-dried baker's yeast + 90 mg cystine + 780 μ g DPNH; Curve B, 2 g washed acetone-dried baker's yeast + 90 mg cystine.

The procedure employed was as follows: 20 g acetone powder was washed twice with 200 ml distilled water, and suspended in 100 ml $M/40$ phosphate buffer, pH 6.2. Ten ml of this suspension (2 g acetone powder) was added with 90 mg cystine and 780 μ g DPNH to a 250-ml filter flask. The volume was made up to 40 ml with $M/40$ phosphate buffer, pH 6.2; 1 ml toluene was added to prevent microbial activity. The flask was stoppered, evacuated through the side arm, and filled with nitrogen. The reaction was stopped by the addition of 2 ml 10% phospho-24-tungstic acid in 5% HCl. After filtration, the volume of the filtrate was made up to 50 ml. A 10-ml aliquot was removed for cystine determination by the Shinohara method, and the remaining 40 ml was titrated with 0.005 N iodine.

⁴TPN was generously provided by the Armour Laboratories, Chicago, through the courtesy of Lawrence L. Lachat.

Since it is known that the action of many antibiotics can be reversed by cysteine, it was thought that this enzyme system might be affected. However, cysteine reduction was not inhibited by streptomycin, fradecin (10), or penicillin.

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Veralbidine, a New Alkaloid from *Veratrum album*

A. Stoll and E. Seebeck

Research Laboratories of Sandoz Ltd.,
Basel, Switzerland

After cautious extraction of *Veratrum album* and working up of the alkaloids, it was possible to isolate the already known bases protoveratrine, jervine, and rubijervine. From the mother liquors, by crystallization from ether, we were able to separate a new alkaloid for which we propose the name "veralbidine." Pure veralbidine crystallizes from dilute acetone in pentagonal plates, from dilute methanol in prisms, and from ether in bunches of fine needles. The crystals melt between 181° and 183° C and exhibit a specific rotation of $[\alpha]_D^{20} = -11.7^\circ$ in pyridine and $[\alpha]_D^{20} = +5.4^\circ$ in chloroform. In 84% sulfuric acid, veralbidine gives a colorless solution. It is sparingly soluble in ether, alcohol, and acetone and insoluble in water. It dissolves readily in chloroform. Veralbidine is irritating to the nasal mucosa, causing sneezing.

The empirical formula of the new alkaloid, as determined by chemical analysis, is $C_{37}H_{61}O_{12}N$. For analytical purposes the alkaloid was dried at 110°.

Required: C, 62.44%; H, 8.57%; N, 1.97%.
Found: C, 62.21%; H, 8.53%; N, 2.14%.

Veralbidine yields a crystalline thiocyanate which melts at 235°–236° with decomposition and frothing. It is readily soluble in methanol and acetone, but sparingly soluble in water. The analytical figures obtained after drying at 110° agreed with the empirical formula $C_{37}H_{61}O_{12}N \cdot HNCS$.

Required: C, 59.26%; H, 8.05%; N, 3.64%; S, 4.16%.
Found: C, 59.04%; H, 8.09%; N, 3.59%; S, 4.09%.
C, 59.10%; H, 8.17%; N, 3.54%.

Veralbidine also yields a crystalline hydrochloride which is readily soluble in alcohol and water. The

hydrochloride melts at 250°–251° with decomposition and frothing. Empirical formula, $C_{37}H_{61}O_{12}N \cdot HCl$.

Required: C, 59.43%; H, 8.29%; Cl, 4.73%.
Found: C, 59.32%; H, 8.45%; Cl, 4.61%.

It is intended to give a more detailed report on the constitution and pharmacological action of veralbidine at a later date.

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The Effect of Experimental Stress upon the Photically Activated EEG¹

George A. Ulett and Goldine Gleser²

Department of Neuropsychiatry,
Washington University School of Medicine,
St. Louis, Missouri

In the search for neurophysiological concomitants of mental processes it has seemed worth while to augment electroencephalographic investigation with the use of the stimulus of intermittently flashing light (1). The ability of such photic stimulation to drive the brain waves was described in 1934 by Adrian and Matthews (2). Such stimulation produces visual sensations (Prevost-Fechner-Benham effect) and a variable dysphoria. Walter (3) has made the observation that the type of brain response produced seems at times to vary in a complex manner with alterations in the subject's mood and that EEG responses appearing at a harmonic of the stimulus frequency might increase at the expense of the primary response. The ability of photic stimulation itself to produce mood changes (1, 3), however, renders such isolated disclosures difficult of interpretation, and hence prompted our investigation of changes in the photically stimulated EEG in subjects whose mental state was deliberately altered under laboratory conditions.

Ninety-six subjects 18–35 years of age were used in this procedure. They were divided into three groups. Groups I and II were selected from a larger sample studied for "anxiety-proneness" by psychiatric and psychological examination (4). Group I consisted of 30 subjects judged least likely to develop symptoms of anxiety under stress. Group II was composed of 25 psychiatric patients with diagnoses of psychoneurosis or character disorder in which anxiety was the predominant symptom. These two groups were placed under an experimental anxiety-producing situation in an attempt to determine whether such stress could affect the photically driven EEG and whether the two groups might react differently.

Group III (41 subjects) was the control group, consisting of experimentally sophisticated medical

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²The technical assistance of Rosemary Baessler and Ruth Ellerman is gratefully acknowledged.

students and hospital staff who were known to be without gross psychiatric disturbance. They were subjected to photic stimulation only, without the added experimental stress.

The experimental procedure required approximately 30 min. Following the recording of the basic EEG all subjects were exposed to intermittent photic stimulation at a frequency of 14 flashes/sec. After an initial 3 min the stimulation was interrupted. Instructions for the ensuing procedure were then given. Different instructions were given to several groups:

- a) Groups I and II were told that during photic stimulation they would have a variety of subjective sensations. They were told that these were known to the experimenter [untrue!] and that they would be called upon to report these experiences briefly and correctly in response to a bell rung at 15-sec intervals. They were informed each time of the correctness or incorrectness of their answers and told that as an incentive to correct reporting an electric shock would be administered if they gave 10 incorrect replies. The replies were then graded in a predetermined fashion, and all subjects received a shock to the hand after their twentieth (i.e., tenth incorrect) response. The procedure was repeated a second time but stopped just short of another shock.
- b) The control groups were exposed to the public stimulation for an equivalent length of time but without experimental stress. Group III_A was told: "Relax, keep your eyes open, and look at the screen." Group III_B was told: "We would like to know what you experience as you look at the light flashing on the screen. You will be asked every few seconds to report as briefly as possible. Accuracy is not important and please be brief."

Photic stimulation was again introduced, and after 1 min recording Groups I and II were subjected to the stress situation for a period of 10 min. At the end of this period, photic stimulation continued for an additional 5 min, but the subjects were informed that they could relax, there would be no more bells or shocks, and they need give no more replies. The controls were recorded for an equivalent length of time.

The EEG's were recorded from a standard placement of bipolar right parieto-occipital needle electrodes made with reference to midline and inion. The critical occipital lead was placed 1 cm above and 1 cm to the left of the inion. All subjects were recorded with eyes open and were seated behind a large opal-glass screen placed some 6-12 in. from the face. The light stimulus was from a tungsten-filament source. It completely filled the subject's visual field with a circle of light of 200 ft-c maximum intensity. This light was interrupted at a rate of 14 flashes/sec by a pendulum-type episcope. The EEG, recorded through Grass Model II amplifiers, was electronically analyzed by a modified, Walter-type electronic brain wave analyzer which permitted an accurate analysis, by 10-sec epochs, of all changes in power (product of amplitude and number of waves) in the 14-c/sec band of the EEG, as recorded before, during, and after photic stimulation at this frequency.

The brain wave response to photic stimulation was

determined by measuring the deflection of the analyzer pen for the 14-c/sec band of the brain wave for representative 10-sec periods during the time of photic stimulation, using as a base line the pen deflection for this band of the brain wave taken with eyes open and without stimulus. Such response is herein called "driving."

The average driving response of Groups I, III_A, and III_B is shown in Fig. 1. Points on the ordinate indicate average millimeters of the analyzer pen deflection. These in turn are directly proportional to the groups' activity in the 14-c/sec band of the EEG at representative periods of time. The period intervals A, B, and C, with their appropriate subnumerals, indicate, respectively, the resting, stress, and post-stress periods of the experiment as previously described. The black line indicates the stressful period, and the arrow the time of shock for Group I.

From Fig. 1 it appears that the experimental group (I), during stress, showed a considerably lower response to intermittent photic stimulation as compared with the control subjects. The difference is even more notable since their driving previous to stress (A₁ and A₂) was the highest. However, it should be pointed out that individuals vary considerably in the extent to which the brain wave may be driven at a given frequency, and the distribution of driving is greatly skewed in that a small number of individuals give very high responses. Also, the amount of response for a single individual fluctuates considerably from time to time, and this fluctuation is greater for high levels of driving. Group averages are affected by large values and may not at all reflect the modal trend.

In order to obtain less skewed distributions with more homogeneous variance, from group to group, and a more accurate picture of group trends, a transformation was made to the square root of the measure of driving. The average values for this transformed variable when the groups were equated as to original driving level (A₂) are shown in Fig. 2. These values were used for all tests of significance. It may be seen that although the differences between the groups are now reduced the general trends persist.

For Group I there was a significant drop in driving level between the response at A₂ and the corresponding response during the period of stress (B₂ through B₆). No such decrease in response was obtained for Groups III_A or III_B. The average response for these two groups was practically identical, indicating that verbalizing in itself did not affect photic driving. The difference between the average change in response for Group I and the change in response for Groups III_A and III_B combined was significant at the 5% level. We can therefore conclude that for normal subjects the introduction of experimental stress tends on the average to lower the driving response. Fig. 3 illustrates this point by means of representative strips taken from the EEGs of an experimental and a control subject at appropriate points in the procedure.

The EEG response of the patients (Group II) was compared with that of the non-anxiety-prone experi-

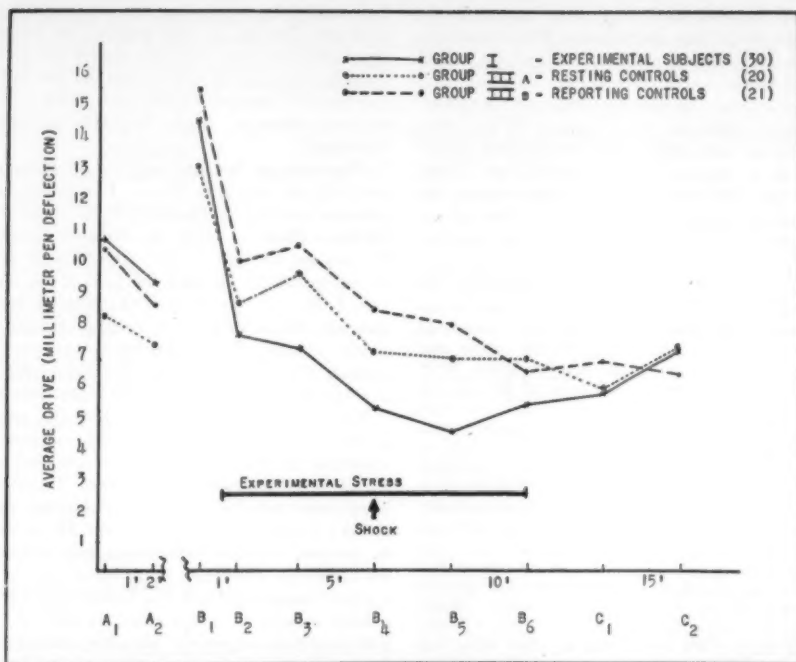


FIG. 1. Average EEG driving response to photic stimulation at 14 c/sec for experimental subjects before, during, and after stress, and for their controls without stress.

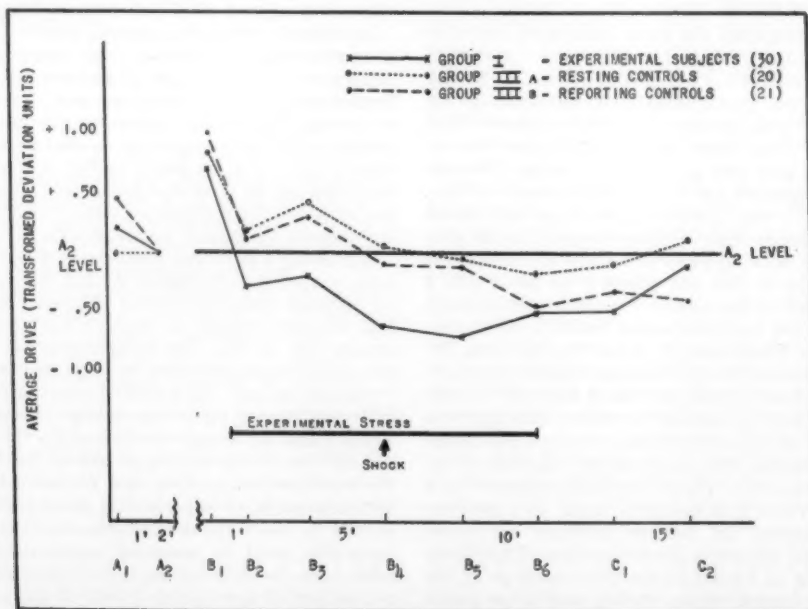


FIG. 2. Square root of average EEG driving response adjusted for differences in initial driving level for experimental subjects before, during, and after stress, and for their controls without stress.

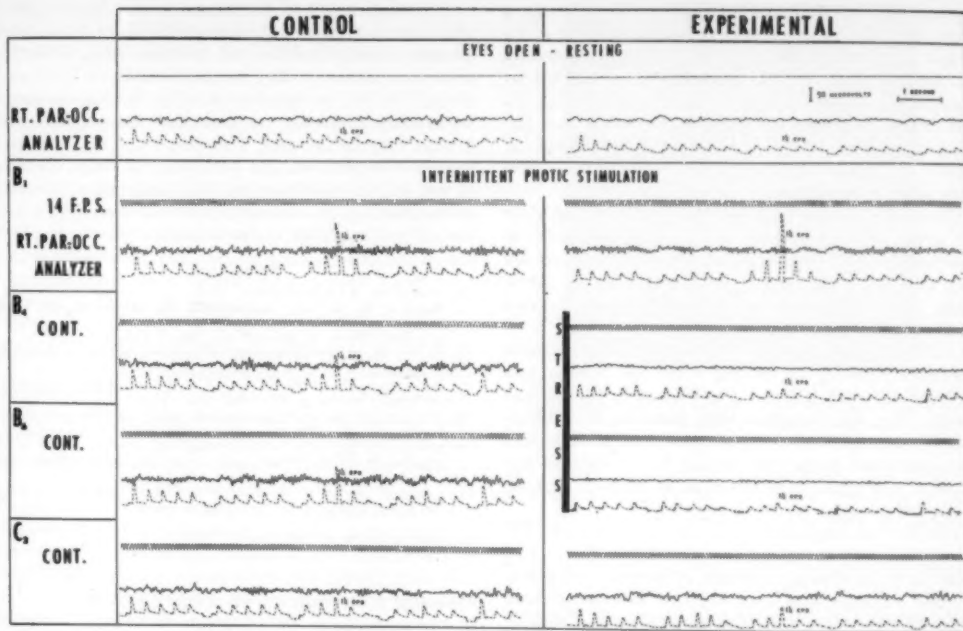


FIG. 3. Representative samples of EEG records from an experimental subject exposed to stress and a control at corresponding periods of rest and photic stimulation.

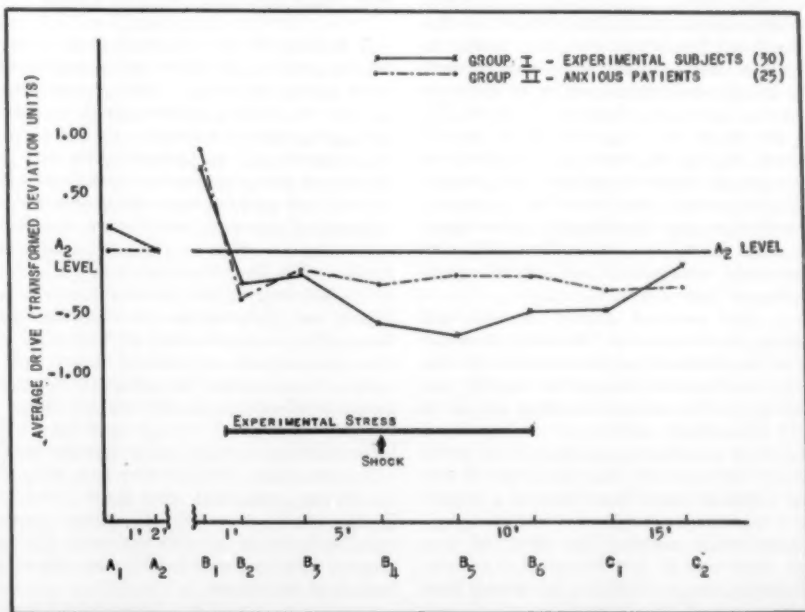


FIG. 4. Square root of average EEG driving response adjusted for difference in initial driving level (A₂ level) for experimental subjects and anxious patients before, during, and after stress.

mental subjects (Group I). Both of these groups, when subjected to experimental stress, showed a decrease in driving below their original level. However, the average drop for the patient group was not as pronounced as for the experimental subjects (Fig. 4). The difference between these two curves was not significant, and yielded no measure for differentiating between patients with anxiety and individuals who were not anxiety-prone.

Group I showed a considerable rise in driving after the stress period was over, so that at C_2 they were at the same or a slightly higher level than the normals who reported their sensations while under no stress (Fig. 2). The increase in driving between B_0 and C_2 for Group I was significant beyond the 5% level ($d = .393$, $\sigma = .161$, $t = 2.44$). Thus the normal subjects showed a recovery in driving after the tension was removed. No such increase was evident in the patient group (Fig. 4). Unfortunately, however, this difference in response was not discovered until all data had been collected; hence, we do not know whether the patients also would have shown an increase in driving if allowed a longer period of recovery.

The driving response at the second harmonic (28 c/sec) was also examined for all groups. There was found to be an average increase in harmonic response in those subjects who were exposed to experimental stress. However, the control subjects showed a similar tendency toward increased response during prolonged stimulation, and thus this phenomenon could not be attributed to the stress situation per se.

From our work it appears that the occipital rhythms induced by intermittent photic stimulation are disturbed by emotional tension in a fashion similar to that in which such stress produces α -blocking. In both instances the synchronized basic pattern is disturbed and the amount of recorded activity is decreased. The mechanisms by which such interruption is accomplished are not fully known, but one assumes from observations such as those of Gellhorn (5), Sapirstein (6), and Jasper (7) that, with the production of anxiety, discharge from diencephalic regions interferes with cortical mechanisms of synchronization by occupying neuronal circuits that are otherwise producing a resting or driven beat.

The finding that screened control subjects and anxious patients do not show a differential decrease of response in the photically activated EEG with the introduction of experimental stress is not entirely unexpected. Malmö (8, 9) reported negative results in attempting to differentiate patients from controls on the basis of amount of α -blocking accompanying painful stimulation. It is possible that the stress of our experimental situation could have induced a degree of heightened attention or "vigilance" in the experimental subjects which matched the effect of any anxiety that appeared in the chronically anxious patients. Vigilance may, as Liddell (10) stated, be a precursor of anxiety. If this be true its induction in the experimentally stressful situation would hinder the differentiation of our two groups.

The relationship of the neural mechanisms responsible for the photic driving response to those that produce α -activity is as yet undetermined. Observations in which a resting α can coexist relatively unchanged with the appearance of a driving response at another frequency suggest that independent cell groups may be at work. The present study does not answer this problem but does suggest that, whether or not such mechanisms use morphologically different or identical units, at least they react similarly when the subject is placed under emotional stress.

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Melting Phenomena of a Surface of Monomolecular Thickness¹

D. E. Beischer

U. S. Naval School of Aviation Medicine,
U. S. Naval Air Station, Pensacola, Florida

A number of observations points to the fact that the surface deviates in its melting behavior from matter in bulk. Lord Kelvin (1871) was the first to recognize that the melting point of the first ordered molecular aggregations is lower than that of bigger crystals. This lowering of the melting point with decrease in the size of the particles, corresponding to an increase of the total surface, was often observed thereafter (Ostwald, Freundlich, and Haber). Another group of experimenters noticed that substances absorbed on porous solids like silica may melt, in extreme cases, 40° below their regular melting points (1). Recently Hüttig and Lichteneker (2) observed that the surface melting of metal layers 10⁻⁴ cm thick takes place at a temperature considerably lower than the true melting temperature, the difference sometimes being several hundred degrees. Stranski (3) found a "rounding off" which removes rough spots on a solid surface before melting, forming a new "crystal face."

Previous work of this author (4), using radioactive monolayers, suggested that these layers would be ideally suited to investigate the phase transition of the topmost layer of a solid material. The radioautographic technique was found to be extremely helpful in such investigations.

¹ Opinions or conclusions contained in this report are those of the author. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department.

The radioactive monolayers were prepared and transferred to a solid substratum by using the Langmuir-Blodgett method (5). Mica plates, slightly scratched on the surface by a fine needle, were used as a convenient supporting material for the layers. They were dipped under a surface of distilled water which was later covered by a monolayer of C^{14} -labeled stearic acid. In preparing this monolayer triercesyl phosphate was used as piston oil. On its way out of the water the mica surface takes up the monolayer from the water surface and is covered by a homogeneous layer of radioactive stearic acid. Specimens thus prepared were heated in a copper block oven without touching the walls.

The two-dimensional order of the unheated monolayer manifests itself on radioautographs in the form of an area of homogeneous optical density. The scratched signs are not noticeable, as the monolayer stretches like a blanket over all uneven parts of the surface. In heated specimens these signs appear and become gradually more and more visible as the temperature and the heating time increase (Fig. 1). The temperature at which the first inhomogeneity of the radioautograph is noticeable depends greatly on the duration of the heating process. In a series of samples heated 30 min, the temperature was found to be 35°C , and in another series heated 3 min it was 40°C . After a four-month storage of the engraved plates at room temperature (27°C), faint outlines of the marks could be observed. The time of exposure of the photographic plate, usually 110 hr, is not included in the above data since the photographic exposure was performed at the low temperature of 3°C .

This very simple method of observation indicates that the two-dimensional lattice of a stearic acid monolayer becomes unstable well below the normal melting point of the stearic acid (70°C). As the temperature increases, more and more molecules move from their position in the lattice by diffusion or evaporation. They leave holes in the original structure and thus further the phase transition solid-liquid. The diffusing molecules come to a rest at points on the surface where they are bound chemically. In an earlier study (4) the rims of scratches, on which the aluminum atoms of the mica structure are accessible, were found to be the places where diffusing stearic acid molecules are immobilized by formation of aluminum stearate. This method is very sensitive, since small accumulations of a radioactive substance are easily noticeable on the otherwise homogeneous background of the radioautographs.

Two additional observations confirm the above-mentioned results. In a quantitative study of surface diffusion of stearic acid on mica, this author (4) found that the surface diffusion coefficient D_s at 50° and at 60°C was 1.1 and $2.8\text{ cm}^2\text{ sec}^{-1}$, respectively. These values are greater than the values normally found for volume diffusion coefficients of substances in solids. They are of the magnitude of diffusion coefficients in liquid diffusion media. Furthermore, the $\log D_s$ vs. $1/T$ relationship does not show a change in direction at

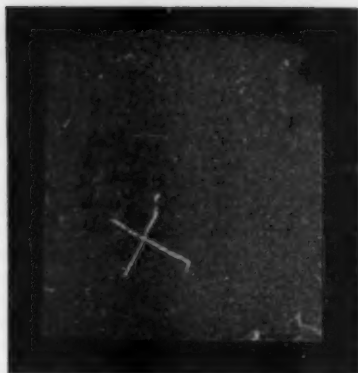


Fig. 1. The melting process of a monolayer is indicated by surface diffusion of the tagged molecules to scratches (cross) where they are immobilized by chemical binding to the supporting material.

the melting point of the stearic acid. This indicates that the monolayer has no phase transition at the temperature characteristic for the melting point of the bulk material.

An explanation of this special behavior of the surface can be attempted, based on the widely accepted theory of the melting process given by Lennard-Jones and Devonshire (6). This theory considers the melting process as an order-disorder transition based upon effects in the immediate neighborhood of the atoms. The neighborhood of molecules in the surface deviates so much from the neighborhood of molecules inside the phase that a special behavior of the phase transition is understandable. The molecules in a complete monolayer are bound to each other in two directions only. In addition, there is a certain influence on the film by the supporting material. All in all, the amount of translational energy which must be made available to render the two-dimensional lattice unstable will be smaller than in the three-dimensional case. The order-disorder transition will take place in the surface at a lower temperature than inside the phase. Lennard-Jones (6) has already suggested that the migration of surface atoms may be the first step of melting of a solid.

The experiments described above reveal still another phenomenon of surface melting. The sharp melting point of matter in bulk, which is so characteristic for a pure substance, could not be found in the phase transition of a monolayer of stearic acid. Similar observations had already been made by Adam (7). He reported that the melting of a solid film on a liquid surface is rarely observed to be sharp. The transition in the monolayer on solid and liquid substrata occurs gradually in a "melting interval," with the time as an additional factor. The single molecules break from their position in the two-dimensional lattice at a rate depending on the statistical nature of the energy available locally. The sharp melting point of material in bulk requires for its explanation the additional as-

sumption that less energy is necessary to move several molecules out of their places in the three-dimensional lattice than to move the same molecules singly. The melting behavior of the material in bulk is determined by cooperative phenomena connected with the long-range order of the molecules in the solid state, whereas the behavior of the surface seems to depend more on the interaction of the neighboring molecules only.

The great importance of the surface of a solid body in all its communications with its surroundings makes surface research a vital part of our endeavor to understand the physical behavior of solid matter. The new possibility of observing the behavior of the topmost molecular layer of solids by radioautographs will be beneficial to a wide variety of experimental research and theoretical discussion. The application of this

method on the observation of the phase transition is an example. It confirmed earlier observations of the melting phenomena of a surface in a more direct way.

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Manuscript received January 25, 1952.

Comments and Communications

Zoological Nomenclature

NOTICE is hereby given that, as from October 15, 1952, the International Commission on Zoological Nomenclature will start to vote on the following cases involving the possible use of its plenary powers for the purposes specified in brackets against each entry. Full particulars of these cases were published on April 15, 1952, in the *Bulletin of Zoological Nomenclature*, those relating to cases (1) to (4) in Part 5 of Vol. 6, those relating to cases (5) to (18) in Parts 7/8 of Vol. 7.

- 1) Meigen, 1800, *Neuvelle* classification [suppression].
- 2) *Lysippe* Kinahan, 1858 (Class Crustacea) [validation].
- 3) *Cummingella* Reed, 1942 (Class Trilobita) [designation of type species].
- 4) *Dionide* Barrande, 1847 (Class Trilobita) [validation].
- 5) Vol. 1 of Cramer's *Uitl. Kapellen*; Schiffermüller's "Wiener Verzeichniss;" Fabricius' *Syst. Ent.*; Vols. 6 and 7 of the *Naturforscher*. [relative to priority for names of butterflies in].
- 6) *Naucoris* Geoffroy, 1762 (Class Insecta, Order Hemiptera) [validation].
- 7) *geoffroyi* Leach, 1817 *Coriza* (Class Insecta, Order Hemiptera) [validation].
- 8) *Sand erab* [trivial name for].
- 9) *Acomea* Eschscholtz, 1833, and *Acomea* Hartmann, 1821 (Class Gastropoda) [settlement of problem relating to].
- 10) *Petalifera* Gray, 1847 (Class Gastropoda) [validation, if name found invalid].
- 11) *punctata* Cuvier, 1803, *Aplysia* (Class Gastropoda) [validation].
- 12) *Ammonia* Brünnich, 1771 (Class Cephalopoda or Rhizopoda) [suppression].
- 13) *Encrinus* Schulze, 1760 (Class Crinoidea) [validation].
- 14) and 15) *Archaeocidaris* McCoy, 1844, and *Pholidocidaris* Meek & Worthen, 1869 (Class Echinoidea) [validation].

- 16) *Eriechinus* Pomel, 1833 (Class Echinoidea) [suppression].
- 17) *Odobenus* Brisson, 1762 (Class Mammalia) [validation].
- 18) *Chinchilla* Bennett, 1829 (Class Mammalia) [determination of type species].

Comments on the above cases should be sent as soon as possible to Francis Hemming, Secretary to the Commission, 28 Park Village East, Regent's Park, London, N. W. 1, England.

FRANCIS HEMMING

Secretary to the International Commission
on Zoological Nomenclature

Salivary Amylase Inhibition

SEVERAL papers have appeared recently describing an inhibition of salivary amylase by indole derivatives (1,2) and several plant hormones (3,4). This was rather surprising to us, for during our study of the crystalline amylases (5-7) incidental work was done in the presence of similar substances without any observable effect. We therefore thought it necessary to clarify this point.

Both crude human saliva and crystalline human salivary α -amylase (6) have been used. The amylolytic power has been determined at 20° C by a redoximetric method (8), using Sumner's 3-5 dinitrosalicylic acid (9), as well as by a method based on the change of color of the starch-iodine complex (10). The latter method, however, is not suitable in the presence of indole derivatives, as these compounds use up the iodine, a large excess of which must therefore be added. The substrate, a 1% solution of Zulkowski starch,¹ was buffered at pH 6.90, and the determination made in presence of 0.0067 M NaCl. The following substances have been tested for their influence

¹ Prepared in our department by R. Menzl.

on the amylolytic action, in concentrations ranging from 0.01 to 0.0001 *M* (covering approximately the range of concentrations used by the previous authors): tryptophane, proline, nicotinic acid, β -indole acetic acid, β -indole propionic acid,² α -naphthalene acetic acid,³ and 1-4 dichlorophenoxyacetic acid.⁴

None of these compounds has shown the slightest inhibiting power under the above-mentioned conditions. It is therefore certain that human amylase is not inhibited by the indole derivatives and other plant hormones that have been mentioned.

ED. H. FISCHER
J. FELLIG

Department of Organic Chemistry
University of Geneva

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² All the preceding substances are pure biochemicals from Hoffmann-La Roche Inc., Basel.

³ Prepared in our department.

⁴ From American Chemical Paint Co., Ambler, Pa.

Isolation of Ascorbic Acid and Rhamnosides from Sea Water

THE presence in sea water of a substance that is physiologically active in oysters and that can be measured photometrically with *n*-ethyl carbazole has been reported by Collier, Ray, and Magnitzky (1). Comparison of the *n*-ethyl carbazole absorption spectrum formed in sea water with spectra of pure carbohydrates led to the conclusion that more than one carbohydrate was taking part in the determination. Methods to isolate and identify the compounds were then sought.

The carbohydrates were removed from sea water onto a column of activated charcoal, as described by Whistler and Durso (2). They were then removed from the column by elution with ethanol. Evaporation of the eluate gave two white crystalline compounds, which were separated by their different solubilities in 50% ethanol. The substance that precipitates in 50% ethanol, as yet unidentified, gives some indication of being a rhamnoside.

Evaporation of the alcohol-water mixture produced a crystalline compound which, in water solution, gave an ultraviolet absorption spectrum similar to that reported for dehydroascorbic acid by Herbert, Hirst, Percival, Reynolds, and Smith (3).

In order to study the similarity between the absorption spectra more closely, we prepared a solution

of dehydroascorbic acid by oxidizing ascorbic acid in the presence of Cu^{++} . The absorption spectrum of this oxidation product agreed very closely with that of our compound from sea water, both in water and in 79% H_2SO_4 . The colors resulting from the reaction of the oxidized ascorbic acid and from our sample with 2,4-dinitrophenyldiazine exhibited the same spectra. The amount of sample available was too small to allow any extensive recrystallization and, therefore, any comparison of melting points with those reported in the literature was not feasible.

Absorption spectra from samples of sea water taken in various parts of the Gulf of Mexico agreed closely with the spectra we had run on oxidized ascorbic acid. We concluded from these curves that the vitamin is present in the sea largely in the form of dehydroascorbic acid. The amounts of vitamin as shown by the absorption spectra did not agree with the calculated amounts of carbohydrate found by the *n*-ethyl carbazole method. The discrepancy is probably due to the as yet unidentified "rhamnoside," which shows some color with *n*-ethyl carbazole. This "rhamnoside" is by far the most abundant carbohydrate in sea water. We have found concentrations as high as 0.1 g/l of the "rhamnoside" from inshore waters.

PETER J. WANGERSKY

Gulf Fishery Investigations
U. S. Fish and Wildlife Service
Fort Crockett, Galveston, Texas

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Experts' Biases about the Older Worker¹

IN OUR industrial economy, which is characterized by rapid technological change, increasing mechanization, and increasing specialization, youth and speed are at a premium. The overemphasis on youth is accompanied by a corresponding underestimation of age, with the result that individuals are fearful about aging. This value system has given rise to complaints and erroneous beliefs about the abilities, skills, and personality structure of the older worker.

During the past year the attitudes of several groups toward the older worker were investigated. The groups differed in age, educational background, and socioeconomic status, and they included undergraduate students, graduate students, middle-aged nonprofessional workers and their wives, and retired men and women living in the community and in homes for the aged. Attitudes were measured by their agreement or disagreement with a questionnaire of 51 statements about the older worker. Some of the statements covered physical decline; others covered mental decline; still

¹ Retirement and Adjustment Series: Number 9. Sponsored cooperatively by the Institute of Adult Education and the Institute of Psychological Research, Teachers College, Columbia University.

others were concerned with resistance to new ideas and procedures, reaction to criticism, attitude toward retirement, attitudes toward the younger worker, etc. All the statements were oriented in terms of disability. Those dealing with physical changes with age have a basis in fact, since there is no doubt that certain changes do occur with age, such as the loss of visual and auditory acuity, reduction of strength and endurance, and retardation of reaction time. Beyond the age of 45 there is a reduction in physical reserve, and there may also be a narrowing range of adaptation. However, the known facts about aging indicate that the physical changes are gradual and vary widely among individuals. Moreover, some of the losses in physiological capacity may be compensated for by the use of glasses or hearing aids, or by modification of work tasks. Apart from the items dealing with physical changes, most of the statements in the questionnaire are not supported by any experimental evidence. They are beliefs, misconceptions, and stereotypes about the job performance of the older worker.

The responses of the groups listed above indicate a negative attitude toward the older worker. Both young and old subscribe substantially to erroneous notions, although graduate students do not accept the beliefs as readily as the other groups studied.

Recently a national meeting was called to discuss problems of the older worker and his retirement. The participants, who included representatives of management, labor, government, medicine, social work, and universities, were individuals with a great deal of experience and interest in the problems of the older worker. The questionnaire described above was given to them in order to determine to what extent a highly selected group of this kind would agree with the beliefs about the older worker. Only 35 of the 75 participants filled out the questionnaire, despite the fact that the president of the conference had explained its purpose and had asked for full cooperation. The average age of the group was 46 years, with a range from 30 to 70 years.

The results, which should be interpreted with considerable caution because of the small number of cases, indicate that the respondents subscribed to fewer misconceptions about the older worker than do any of the groups referred to above. However, more than 30% exceeded the mean number of stereotypes subscribed to by graduate students. More than 80% of the respondents agreed that older workers take longer in getting over illness; 65-75% agreed that they take longer in getting over injuries, are more interested in security than job advancement, look to the past, and need more time to learn new operations; 50% agreed that older workers resist new ways of doing things. On the other hand, none of the respondents subscribed to the beliefs that older workers fail in emergencies, make many errors, are interested only in putting in their hours, spoil much of their work, and quit jobs frequently.

There were wide and interesting differences among the various groups represented at the conference. The

number of beliefs subscribed to by those representing the universities, government, and labor was considerably below the mean for the total group, whereas the number accepted by those representing management, medicine, and social work was considerably above the mean. For the labor representatives, a higher proportion agreed that older workers need longer and more frequent rest periods. For the social workers, a higher proportion believe that they take jobs away from younger workers, are unsure of themselves, increase production costs, are unable to smooth out disagreements, cannot concentrate, are critical of younger workers, need more time to learn new operations, are not physically able to keep up with the work, resist new ways of doing things, look to the past, and are suspicious of other workers. For the physicians, a higher proportion think that older workers are slow, fail to keep up with changing methods of work, have a high rate of absenteeism, lose jobs often, get all the breaks, take credit for the work done by younger men, have difficulty in planning their work, are paid too much for the work they do, increase costs of pensions for employers, are slow to catch new ideas, are mentally unable to keep up with the job, are difficult to work with, and cannot listen to other people's complaints without getting irritated. For management, a higher proportion agreed that older workers cannot win the confidence and loyalty of fellow-workers, are in a rut, show poor judgment, have no ambition, cannot supervise others well, get occupational diseases more often, are more interested in security than job advancement, will not carry out plans assigned by supervisors, and keep younger men from getting ahead.

Within the obvious limitations of the data, the replies to this questionnaire suggest that individuals generalize about the older worker in terms of their own experience and orientation. The representatives from universities, government, and labor, who, in their daily work, look for and are impressed with the positive rather than the negative aspects of aging, subscribe less to the stereotyped opinions than the management, social work, and medical groups, which tend to see the negative rather than the positive aspects of aging. The labor representatives, whose orientation is in terms of job security and job protection, see the older worker as one in need of such protection. The social workers, who work with individuals who have adjustment problems, see him as one who is insecure, rigid, deteriorated, and difficult to get along with. The representatives of management, who are concerned with production, see the older worker as one who has no ambition, and who presents difficulties in supervision. The physician, whose orientation is in terms of pathology, views him as an individual who is slow, rigid, and unproductive.

Individuals who are experts in aspects of the aging process appear to have projected their specialized experiences into their responses to the statements in the questionnaire. But it is the bias of experience with substrata of the total aging population that gives rise

to various points of view, which are not incorrect for the substrata but lead to genuine misconceptions for the class as a whole. For instance, although two thirds of the aged are physically able to take care of themselves socially and economically, and are able to function psychologically, physicians may popularize quite a different view as a consequence of their examination of the other third.

The meager data from this study suggest the need for orienting experts about potential biases from their own experiences. There is need for a campaign to change the attitudes of the public toward the older worker. Such an educational campaign should stress

the normality of the physical and psychological changes that come with age, and that should not be confused with deterioration. In view of the fact that the number of older workers in the labor force, already large, will continue to increase in the future, a change in attitudes toward the older worker is necessary if they are not to become a severe drain on the economy because of discrimination in employment. The experts seem to be in especial need of orientation.

JACOB TUCKMAN
IRVING LORGE

Teachers College, Columbia University

Book Reviews

London Essays in Geography. Rodwell Jones Memorial Volume. L. Dudley Stamp and S. W. Woolridge, Eds. Cambridge, Mass.: Harvard Univ. Press, 1951. (Published for the London School of Economics and Political Science.) 351 pp. \$5.00.

The 17 essays comprising this memorial volume were prepared by colleagues and former students of Professor Jones. The authors received most of their training and developed their specialized interests in the King's College and London School of Economics joint School of Geography which Rodwell Jones, in cooperation with W. T. Gordon, of King's College, was largely responsible for organizing in 1921-22. It was due to his patience, wisdom, and experience that the new venture was able to surmount the difficulties encountered in the first few years of operation. The school developed a broad coordinated approach to geography—economic, historical, and physical—designed to meet the specialized needs and capabilities of the two colleges, to build a sound academic treatment of the subject, and to put it upon a firm academic foundation.

The essays cover various aspects of geography. All are well written, in language that should present no difficulties to the understanding layman. Some, like Kenneth Hare's "Climatic Classifications," are technical and functional in approach, designed for the specialist. Others, such as Beaver's "Development of the Northamptonshire Iron Industry, 1851-1930," or Gordon's "Severn Waterway in the Eighteenth and Nineteenth Centuries," which effectively integrate physical, economic, and historical data, are excellent examples of historical geography and closely resemble the Rodwell Jones approach to the subject. Dudley Stamp's "Applied Geography" does a superb job of demonstrating in a practical fashion the role of geography in land-use planning. One could wish that the volume contained more essays of this type covering economic, political, and social problems. In his approach Stamp clearly demonstrates "the application of geographic principles and methods to the problems of town and

country, the actual methods employed by the geographer in attacking his problem," and the basic goals the study should achieve.

Geographers the world over will find the essays stimulating and helpful. Their variety will satisfy needs of both specialists and generalists. To social scientists they present a clear picture of how geographical factors can contribute to the solution or interpretation of many types of problems.

As a memorial to "a loved and respected friend and teacher" the volume is somewhat disappointing. Too little emphasis is given to "the man"—the man who contributed so much to the development of geography in the University of London and, particularly, to the joint efforts of the London School of Economics and King's College.

Rodwell Jones was not a prolific writer, but what he did publish is characterized by a very high standard of scholarship. It is unfortunate that the editors did not see fit to include a bibliography of his essays as well as of his books, a reprint of his stimulating inaugural address made in October 1925 when he succeeded H. J. MacKinder as head of the Department of Geography in the London School of Economics and professor of geography in the University of London, and a portrait. These personal aspects, appropriately highlighted, would have sharpened the picture of the man from whom many students drew inspiration and guidance.

JOHN B. APPLETON

*Office of Intelligence Research
Department of State*

Advanced Engineering Mathematics. C. R. Wylie, Jr. New York-London: McGraw-Hill, 1951. 640 pp. \$7.50.

The increasing extent to which modern engineering technology has availed itself of mathematical tools beyond the calculus is well illustrated by the content of this book. Technically, the material divides into two parts, although the presentation itself is con-

tinuous and logically integrated. The first eight chapters, making up the first part, are a course in linear differential equations with emphasis on time invariant systems and their solution by Laplace transform methods. The second part, Chapters 9 through 14, is a course in complex variables, leading, on the one hand, to the complex integral inversion of the Laplace transform and, on the other, to engineering applications of conformal mapping. A chapter on Gibbs vector analysis, one on numerical analysis, and an appendix covering selected topics in algebra and calculus complete the book.

The text is one that could be used for self-study. The style has classroom informality, without being verbose, and a running account of all manipulative steps in proofs and derivations is provided which is adequate to guide an unsophisticated reader. The text is illustrated by many worked examples, and the student is offered a wide and graded selection of problems for solution. Few of the examples or problems are formal exercises. Most of them illustrate both a mathematical point and a potential application by means of a problem drawn from, or at least in the language of, some branch of engineering.

The author should be commended on maintaining a high standard of mathematical precision, without sacrifice of readability or heuristic explanation.

The book is well made, well printed, and liberally illustrated with excellent diagrams.

The selection of material seems generally good. Omissions in a work of some 600 pages can scarcely be criticized. The reviewer has a serious disagreement with the author concerning the importance of the impedance concept, however. In particular, the author's last sentence on page 95 is simply wrong. This difficulty could be resolved by a transfer of much of the applicational material of Chapter 4 to a point following Chapter 6, expanding the horizon to include analyses of transient behavior by calculation of impedances.

The reviewer would like to make a general comment on selection. The linear mathematics of engineering is a forest which, in all works known to him, is completely obscured by trees. These works, including the present one, are botanical catalogues; each needs at least one chapter on ecology.

In fact, throughout the linear field, one is dealing with a relatively small number of basically geometric concepts. Admittedly, the emphases and the details, in the specific instances of ordinary differential equations, boundary value problems, etc., are varied and essentially so. This, however, is no reason for concealing from the student an underlying unity which does exist. A good introduction to the *geometry* (not the formalism) of finite dimensional vector spaces could provide the language and intuition needed here, but to this reviewer's knowledge no such introduction has yet been made accessible to engineering students. It is his belief that adequate coverage of these ecological, or at least morphological, topics could simplify later presentations to a point where a net sav-

ing in bulk might result. The reviewer would, in any case, include the ecology even at the expense of omitting botanical items from the catalogue.

BROCKWAY McMILLAN

Bell Telephone Laboratories, Inc.

Murray Hill, New Jersey

The Role of Engineering in Nuclear Energy Development. Proceedings of the Third Annual Oak Ridge Summer Symposium, August 27-September 7, 1951. N. F. Lansing, compiler. Distributed by Office of Technical Services, Department of Commerce, Washington, D. C. 509 pp. \$1.40.

The material covered in this volume will be of great value to administrators as well as to research men in engineering schools who want answers to the questions: Just what should be the background of a nuclear engineer? What type of courses should be taken? What are the problems involved in reactor technology and the problems for the practicing engineer in the atomic energy program?

The symposium is divided into four parts. In the first part, T. K. Glennan deals with general problems in engineering and the objectives of the Atomic Energy Commission. This is followed by C. J. Suits discussing some economic aspects of atomic power. L. R. Hafstad describes the atomic energy reactor program, and, finally, J. A. Lane considers the contribution of engineering to nuclear energy development. The second part covers the scientific background, starting with basic concepts of nuclear physics (A. H. Snell). A simplified approach to reactor calculations by A. V. Masket will certainly be valuable for the engineer who wants to become familiar with the problems involved in reactor calculations. This is followed by standards of radiological protection and control, by K. Z. Morgan. This information will be of great interest to the practicing engineer, as well as to anyone organizing a nucleonics program.

Part three covers the engineering aspects. J. A. Swartout discusses chemical problems in the development of nuclear reactors. This is followed by the problems of separation of stable isotopes, materials of reactor construction, heat transfer problems in nuclear reactors, instrumentation in control of reactors, nuclear radiation shielding principles, and disposal of radioactive waste material. This section should be of great interest to the industrial and sanitary engineer.

M. M. Mills, of North American Aviation, presents a discussion of hazards of low power research reactors—a subject for careful consideration by all educational institutions and research laboratories building a small reactor. A survey of reactor types by N. F. Lansing is well illustrated with schematic drawings and photographs of the declassified existing reactors.

The last fifty pages of the symposium are devoted to a panel discussion of the problems in nuclear engineering education. Experts in nuclear technology from Oak Ridge (A. Weinberg and F. C. Vonder

Lage), and university educators (Dean Boelter, Dean Ernst, and Clifford Beck) attempted to clarify the problems of engineering education for reactor technologists or nuclear engineers. Educators as well as nuclear technologists seem to favor experimentation with various types of curricula: a special nuclear engineering program, a solid basic foundation in physics and chemistry, with appropriate courses giving the fundamentals of nuclear physics, tracer techniques, elementary reactor theory, nuclear instrumentation, and radiochemistry. And, as Weinberg emphasized regarding establishment of nuclear engineering courses in engineering curricula: "This can only be attained if each engineering school makes a temporary sacrifice by sending one or two faculty members to an atomic energy installation or industrial organization engaged in atomic energy development to get firsthand experience with the effort."

The engineer as well as the educator will certainly benefit by this summary of the engineering aspects of the atomic energy program. We hope new developments, as they become declassified, will be presented to keep the material up to date.

KARL LARK-HOROVITZ

Department of Physics, Purdue University

The Planets: Their Origin and Development. Harold C. Urey. New Haven, Conn.: Yale Univ. Press, 1952. 245 pp. \$5.00.

The Silliman Lectures at Yale University have in the past led to the publication of two outstanding volumes in the field of astronomy—W. W. Campbell's *Stellar Motions*, based on a 1910 series of lectures, and E. P. Hubble's *Realm of the Nebulae* (1935 lectures). The Urey book is a worthy addition to this distinguished pair. It is a volume written by a competent physical chemist, thoroughly conversant with the relevant areas of astronomy, geophysics, and geology and obviously a master in mathematical and practical physics. It is a book that deserves to be read and studied by everyone who is even remotely interested in the physics and chemistry of the moon and planets as they are today and as they may have been in the past.

Harold Urey has written a book that cannot be read and digested in one or two evenings, since much of the material in it is of a technical nature. In the introductory chapter the author reviews current theories on the origin and development of our solar system. Here he leans primarily on Kuiper's modification of von Weizsäcker's theory, according to which our system of planets came into existence as a result of the collapse of a turbulent solar nebula with a total mass of the order of one tenth that of our sun.

According to Urey's picture, our solar dust cloud was in the earliest stage a small, dark nebula, a globule, not unlike the globules one sees even now projected in abundance against the bright background supplied by diffuse gaseous nebulae—surprisingly most frequently against certain conspicuous, extended, and highly ionized diffuse nebulae. The globule is

supposed to have collapsed gradually to become a proto-star, and as the sun was formed there would then remain behind sufficient matter for the formation of a cool disk of gas and dust, the solar nebula. Since the temperatures in the solar nebula are low at the start, most of it—with the exception of H, He, and Ne—would presumably be in a solid stage. The disk would rather promptly break up into large masses, the largest of them pretty far from the sun.

In a way, Urey's theory is a 1950 version of the planetesimal hypothesis proposed more than 50 years ago by Chamberlin and Moulton, also of the University of Chicago. Urey sees the lunar craters as of meteoric origin and—in agreement with most recent writers on the subject, notably Baldwin—he therefore rejects the volcanic theory for the origin of lunar craters. Accompanying the volume is an excellent composite map of the moon. With this map as a guide, the author analyzes many of the surface features of our moon in terms of planetesimal bombardment. Even the lava-flow features on the moon's surface are assumed to have arisen as a consequence of the melting of the planetesimals themselves.

Urey follows in detail the probable development of the terrestrial planets. After the formation of the sun, the first proto-planet stage is one of low temperature—close to freezing for the earth—with methane gaseous and not condensed in the disk to well beyond the range of Pluto, and with the terrestrial planetesimals largely composed of silicates, water, and ammonia. Ne, H, and He would not be bound and should already have largely escaped from the proto-planet at this early stage. The stage that comes next is one in which the interior temperature of the proto-planet is raised through adiabatic compression. Silicates will be reduced and volatilized, and a large fraction of the gases will escape from the proto-planet, thus increasing the proportion of iron phase in planets like our earth. With the departure of most gases from the proto-planet, the opacity should decrease, and the surface temperature will then begin to drop again. The temperature should then remain at a fairly low value, and this would hardly be changed by further gradual accumulation of mixtures of iron and silicate. The final stage is now approached with, for our earth, 45 per cent metallic iron and 55 per cent silicates, and with the iron gradually sinking to the core.

Urey considers it most likely that the moon was formed from a secondary nucleus within the earth's proto-planet, although he does not rule out entirely the possibility of wholly separate formation of earth and moon and subsequent capture. Under any circumstances, it does not seem likely that the moon has passed through a high-temperature stage. The more volatile solids, which escaped from the earth's proto-planet, have probably been retained by the moon. The moon has mostly silicates and some small admixture of metallic iron, and its composition still may be close to that of the original dust cloud.

The virtues of Dr. Urey's book are many. It repre-

sents the result of a clear and open-minded thinking through of a difficult problem. It is a far cry from the theories involving hot filaments between colliding stars, which held sway not very long ago, to Urey's dust-cloud hypothesis! The principal value of the book probably lies not so much in the fact that it deals with an "up-to-date" theory of the origin of the solar system, as in the approach of a careful following through of the detailed physical-chemical processes that must have taken place as a consequence. One gets the distinct feeling that proponents of future theories on the origin and development of the solar system, who wish to be taken seriously, will of necessity have to examine with care the detailed physicochemical processes that follow from their hypotheses. One only hopes that there may always be enough Ureys in the world with ability, vision, and training equal to these tasks!

The book is well printed and is not tiring to read. As far as this reviewer has been able to judge, it is remarkably free from printing errors and errors in figures, although one cannot help but be amused by the editorial slip on page 123, where the word "retention" is in one prominent place spelled correctly, to be misspelled with equal prominence on the same page on nine pages after that!

BART J. BOK

Harvard College Observatory

Statistical Design and Analysis of Experiments for Development Research. Donald Statler Villars. Dubuque, Iowa: Brown, 1951. 455 pp. \$6.50.

The appearance of another book on statistical methods in these days when statistics seems to be the vogue is noted with interest and hopefulness. This text is an attempt to acquaint research personnel (often lacking in formal statistical training) with the more frequently used techniques of statistical analysis. A wide variety of topics is included: (1) The use of calculating machines; (2) "Student's" t test and required size of sample for the detection of real differences; (3) a discussion of the binomial, Poisson, normal, chi-square, t , F , and other theoretical distributions of use in statistical methods; (4) analysis of variance and the design of efficient experiments; (5) the use of regression (linear and nonlinear) and an introduction to the principles of covariance; (6) quality control charts and the elements of sequential analysis; (7) miscellaneous topics including efficiency studies, components of variance, Sheppard's corrections, and a short note on the Behrens-Fisher test.

In the preface, the author indicates that this book is intended to aid the research worker in properly planning his experimental projects so that statistical methods may justifiably be used in the interpretation stage. A minimum of mathematics is to be used. In general, he does an excellent job of emphasizing the need for good planning. For example, on pages 84-5:

It is desired especially to emphasize that the way the variability should be analyzed is entirely dependent upon the way the experiment was set up. There is only one correct way to analyze a particular experiment. It is predetermined the moment the runs are made. The manner of

replication of the different possible effects is the determining factor. Obviously, use of an incorrect scheme of analysis can lead to erroneous conclusions. Incidentally, as has already been mentioned, if the results of the statistical analysis seem to violate common sense, the chances are great that common sense is right and that an error has been made because of an incorrect subdivision of the error degrees of freedom—one did not have as much replication in the places that the incorrect method of variance analysis implies.

On the other hand, however, the presentation of the techniques, especially analysis of variance, shows a certain lack of sophistication, with the result that incorrect test procedures are sometimes suggested or may be inferred. For example, the second paragraph on page 7 and the second paragraph on page 75 lead one to believe that an interaction mean square is the correct "error" against which main effects should be tested. Such is seldom the case! This matter is better explained later in the text, but it is feared that the damage has already been done. Then, too, at the top of page 69, the impression is given that, if F is significant (in an analysis of variance), one has the right to make t tests for comparing all possible pairs of treatment means. This is generally considered to be poor procedure.

It is unfortunate that Villars has not seen fit to adhere closely to the accepted terminology of statistics, poor though it may be in some instances. The addition of new terms, when no need appears to exist, only adds to the large list of terms and symbols that already awaits the statistical novice. His introduction of "replication degeneracy" seems a misguided effort, indeed. Also, the classification of designs given in Chapter 7 is peculiar. The setting up of two classifications—*simple* ("between and within") and *factorial*—is misleading, since factorials are not designs as the statistician interprets the word. What the author is attempting to do is to classify treatments according to their composition, simple or factorial; and designs as completely randomized ("between and within"), randomized complete block, Latin square, and so on. He adds further to the confusion by referring to a "between and within" design as a "uniform medium" design—another new term to be learned. Other items such as these could be mentioned if time and space permitted.

The reviewer is flattered to be included (a presumption on his part) in the "... small nucleus of agricultural statisticians in Iowa ..." (p. vi) who have paid some attention in the past to small sample (*exact*) statistics. However, he feels that the implication that all other statisticians in America have only recently deviated from consideration of purely large sample (*asymptotic* or *approximate*) statistics and awakened to exact statistics is unjustified. It is realized, of course, that much depends on the interpretation given to the word "recently." In view of this wide latitude of meaning, let us be charitable and assume that people outside Iowa have heard of, and believe in, small sample statistics.

BERNARD OSTLE

Department of Statistics, Iowa State College



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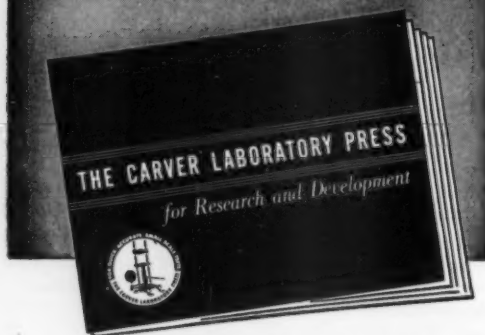
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June 23-25. Forest Products Research Society (Annual). Milwaukee.

June 23-25. Symposium on Military Medicine. Murphy Army Hospital, Waltham, Mass.

June 23-26. American Veterinary Medical Association. Atlantic City.

June 23-27. American Institute of Electrical Engineers (Summer). Nicollet Hotel, Minneapolis.

June 23-27. American Society for Engineering Education. Dartmouth College, Hanover, N. H.

June 23-27. American Society for Testing Materials (Annual). Hotels Statler and New Yorker, New York.

June 23-27. Institute for Annual Review of United Nations Affairs. United Nations, New York.

June 24-26. Heat Transfer and Fluid Mechanics Institute. University of California, Los Angeles.

June 24-27. American Home Economics Association. Convention Hall, Atlantic City.

June 24-27. Medical Library Association (Annual). Lake Placid Club, Essex Co., New York.

June 24-28. Conference on Industrial Physics. Royal Technical College, Glasgow.

June 24-29. American Dairy Science Association. Davis, Calif.

June 25-27. British Society for the Study of Fertility. London.

June 25-28. American Astronomical Society. Victoria, B. C.

June 26-27. Applied Mechanics Conference. University of California, Los Angeles.

June 26-27. Southern Association of Science and Industry, Inc. (Annual). Robert E. Lee Hotel, Winston-Salem, N. C.

June 26-28. Institute on Atomic Energy—Industrial and Legal Problems. University of Michigan Law School, Ann Arbor.

June 26-28. National Science Teachers Association. University of Michigan, Ann Arbor.

June 26-29. Society for the Study of Development and Growth, Symposium on Growth Processes. Williams College, Williamstown, Mass.

June 29-July 2. American Medical Technologists. Hotel Syracuse, Syracuse, N. Y.

June 29-July 5. American Library Association (Annual). Waldorf-Astoria Hotel, New York.

June 30-July 3. American Physical Society (Summer). Denver.

July 1-3. American Meteorological Society (National). Buffalo, N. Y.

July 7-11. International Congress of Dietetics. Royal Tropical Institute, Amsterdam.

July 7-11. International Congress of Physiology and Pathology of Animal Reproduction. Copenhagen.

July 7-11. Society of the Chemical Industry (Annual). Aberdeen, Scotland.

July 7-12. Congress of the International Diabetes Federation. Leyden.

July 7-12. International Conference on Safety in Mines Research. Buxton, Derbyshire, Eng.

July 8-11. British Congress of Obstetrics and Gynecology. Leeds, Yorkshire.

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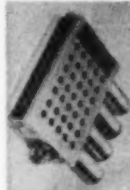
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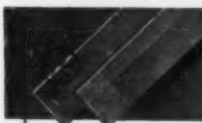
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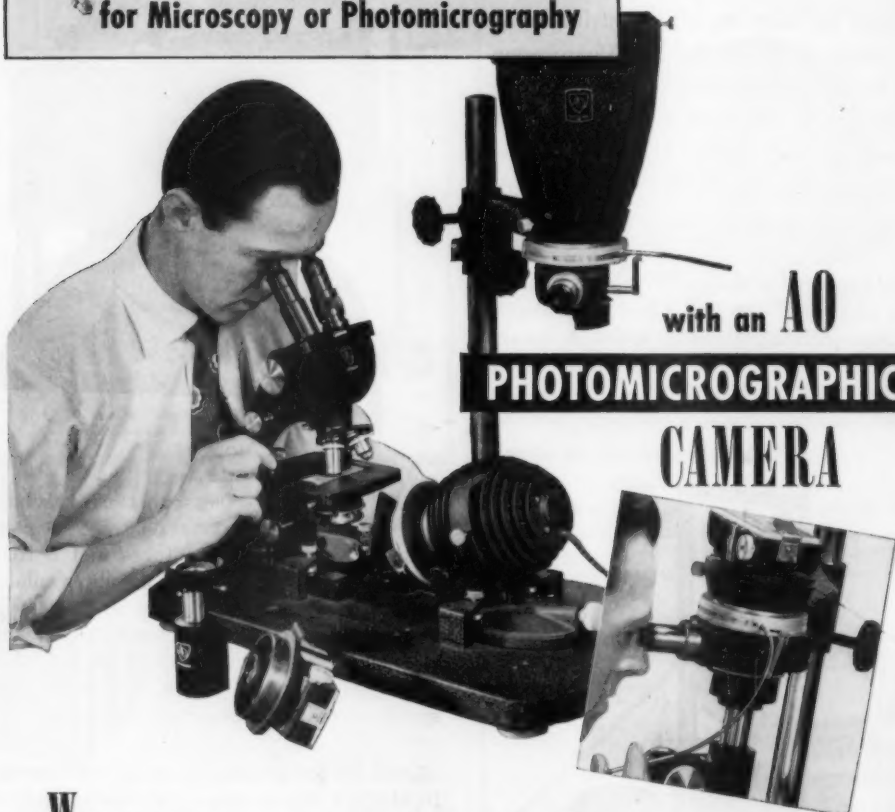
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